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ROYAL COMMISSION ON MATTERS OF HEALTH AND SAFETY ARISING FROM THE USE OF ASBESTOS IN ONTARIO

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Volume XXI B

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THE FURTHER PROCEEDINGS OF THIS INQUIRY RESUMED PURSUANT TO ADJOURNMENT

APPEARANCES AS HERETOFORE NOTED

MR. LASKIN: I think I have an announcement that will ease everyone's burden today, and the announcement pertains to Dr. Gibbs. Dr. Gibbs, who we talked to last night and explained our timing problems suggested it may be unfair both to him and to everyone else to thrust him into the middle of this milieu sometime in the afternoon. In those circumstances he has agreed, and has been good enough, to come back before this Commission at a later time...likely the last week in August, but he has got to check his calendar.

So I hope I haven't put everybody out by working into the wee small hours of the morning.

I didn't know myself until the wee small hours of the morning, but I think probably in retrospect everybody would be a lot happier with that solution.

DR. DUPRE: I congratulate you, counsel.

DR. PAUL KOTIN, PREVIOUSLY SWORN, RESUMES THE STAND

DR. DUPRE: Dr. Kotin, while you were out, Mr. Laskin gave your class the good news that Dr. Gibbs agreed to

DR. DUPRE: (cont'd.) a postponement, which takes some of the pressure of us in terms of time today, and we will be able to, as a result, put our questions at the normal pace rather than trying to speak overly rapidly.

One other announcement before we start, from the chair, apparently there is a maintenance personnel expected around nine o'clock to work briefly on the recording machine. So I will call a five minute coffee break whenever that person appears, around an hour from now.

Counsel?

MR. LASKIN: Thank you, Mr. Chairman.

CROSS-EXAMINATION BY MR. LASKIN, CONTINUED

Q. Dr. Kotin, can we just finish up the discussion we had yesterday on this no-effect level, and let me just summarize one or two things. In your judgement, looking at the biological principles, a no-effect level of exposure, or a threshold, is one of the four relatively common aspects of environmental response. Fair?

A. Yes, sir.

Q. Looking at the epidemiological evidence, do I put it fairly to say you suggest some studies support the proposition there is a threshold, and other studies support the proposition there is no threshold?

A. Yes. In either case there is no measurement at that low end of the curve.

Q. Sorry?

A. I suggest that in either case there are no really substantive measurements at that lower end of the curve.

Q. Then I come to the submission that you made to this Commission last January, which is at tab twelve, can I take you to page three?

A. Yes.

Q. The last sentence in the first full paragraph says, and you have been discussing these responses, and you say,

> "In addition, a no-adverse-effect level of exposure, or threshold, has been demonstrated for the asbestos-related diseases of asbestosis and lung cancer".

Looking at your footnotes, you support the argument on asbestosis by Dr. McDonald's study, and the argument on lung cancer by Dr. Weill's study?

A. Correct.

Q. All right. Is there anything...is there any new evidence between the time you delivered the brief in January, of 1981, and today, which would cause you to change, add to, subtract from that statement in any way?

A. No.

Q. All right. Let me ask you one or two questions: I note, first of all, your omission of mesothelioma from that catalogue?

A. That's correct.

Q. Was that a deliberate omission?

A. Yes, sir.

Q. Is that because there is no epidemiological study from which we can conclude a threshold or no-effect level has been demonstrated?

A. No. The reason is that our knowledge of mesothelioma is much more recent and the circumstances surrounding the diagnosis and verification of mesothelioma are different than for asbestosis and for lung cancer.

It is well to remember that as recently as twenty years ago, twenty-five years ago, one of the most universally-used textbooks on pathology, edited by Professor Willis, even denied the existence of the entity of mesothelioma.

Further than that, mesothelioma is, as I mentioned

A. (cont'd.) yesterday, an uncommon neoplasm. Unlike lung cancer and asbestosis, the criteria for diagnoses are... maybe a little overstatement, but haven't until relatively recently measureable, and perhaps five years, ten years, it has never been fully formulated or crystallized that the tumor itself, the neoplasm itself, is one, both in terms of its histological characteristics and in terms of its location, one that was subject to a degree of confusion, possible confusion, that didn't exist for lung cancer.

Perhaps most eloquent in verifying this has been the fact that in most countries around the world where the issue is being addressed, things like...or groups like mesothelioma panels have been established...the panels consisting of groups of pathologists who by virtue of their special interest and experience have expertise in the diagnosis of pathology, of cancer in general and mesothelioma particularly. So that there is still some confusion as to what really constitutes the actual incidence or prevalence, depending upon the data, of mesothelioma.

As recently as January of this year, Professor Henderson from the University of Southern California, in a presentation to an international cancer conference in New York, at the Hyatt Regency, had invited Peto, Julian Peto from the U.K., to spend some time...Brian Henderson, Chairman of the Department of Preventive Medicine at the University of Southern California...to come and study the Long Beach Naval...take another look at the Long Beach Naval population, and as part of that study, Professor Russell Sherwin, who is the sort of head of the Pulmonary Section of the Department of Pathology at the University of Southern California Medical School, reviewed the diagnoses of mesothelioma.

He arbitrarily divided the cases of meso that were presented to him, from the point of view of pathological verification, into two categories: Those which had a history of exposure to asbestos that were documentable, an occupational history, and those that didn't.

A. (cont'd.) In the paper, if I remember the numbers correctly...and they are published in volume one of the proceedings of this cancer symposium held in January of this year...he felt that he couldn't verify eighty-seven percent of the mesotheliomas in that group which did not have an occupational history, and that other group, he felt that he could not verify the diagnosis of mesothelioma in fifty percent of the cases.

After that observation, I then made a phone call to Dr. Churg, who was then at the University of Southern California... this is Andrew Churg, not his father Jacob Churg, who has also worked in the field, of course...and Andy is the Chairman of the Mesothelioma Panel which is a joint U.S./Canadian panel... and he verified that fifty percent of the cases that came to them were questionably mesothelioma.

In talking to pathology associates on the continent, I really get much the same figure.

Then looking at my own experience in the diagnosis of pathology, I'm part of that great majority that has that fifty percent confusion as well.

So that I'm still uncertain as to what the real attack rate of mesothelioma is, but let me make it very, very clear that I believe there is the entity of mesothelioma, I believe it is diagnosible, and in pathology there are routine ways of handling tissues, for examining them under the microscope, and mesothelioma is one of those tumors where the routine methods are supplemented by additional methods - special stains and the like - and I think it's fair to say when a pathologist has to start looking at special stains, generically, he is in trouble in terms of the specificity of the diagnosis.

That's just one facet of my concern over mesothelioma in terms of the actual validity of the numbers of the rate.

Then one looks at the discussion of mesothelioma

A. (cont'.d) at meetings of pathology societies, at their annual meetings, and again, we are in the midst of, I guess, the first decade of real education of pathologists in terms of meso, so that I'm sure there is a jumbled mess of areas of underdiagnosis of mesothelioma and areas of overdiagnosis of mesothelioma.

So really, I'm not...the numbers are not that reliable when compared with asbestosis and lung cancer.

Q. And that's why, that discussion is why it's not found in the catalogue?

A. Yes, I have no confidence that I can take the same attitude. I would suggest a competent fellow finishing the sophomore year in pathology will diagnose most cases of lung cancer.

Q. Is another facet of the problem in evaluating the significance of the cases of mesothelioma that in many of them we simply don't have any dose measurements...the nonoccupational mesotheliomas?

A. That's correct.

Q. Is it a possibility, in your judgement, that mesothelioma may simply be one of those rare instances...maybe even unique instances...where there is no dose-response relationship?

A. I don't know how to answer a question, 'a possibility,' because I assume in this universe everything is possible.

Do I regard this as sufficiently likely not to exclude it from my deliberations, or to include the fact that it might not. It would be unique. Even for the most exquisitely potent carcinogen we know, the product of aflatoxin, the product of a mold, a dose response exists, so the potency of a carcinogen hasn't, where the data are available, in anyway negated or obviated a dose-response dimension.

Q. Does the animal evidence help us one way or the other on that issue?

A. It does in terms of mechanisms, in terms of the extrapolation of quantitative data from the animal to the man. No, I know of no carcinogen where you can extrapolate quantitative data in the sense that you are speaking of it, to man from animals.

Q. I take it that's really what you said in your article at tab one on page twenty-seven, where you talked about some of the limiting factors in attempting to relate dose response and threshold.

Do I take it, to put in my simple layman's terms, that the animal evidence may tell you whether there is a relationship between say asbestos and mesothelioma, but it won't tell you in man what quantity of dose is or is not likely to produce an excess risk?

A. As you put in your layman's way, you put it perfectly, exactly. There really isn't.

Q. Does that apply not only to asbestos and mesothelioma, but to generally any animal evidence that we have in terms of using it as the situation in man?

A. Well, you can do it...yes, I would say so. But as in every other biological phenomenon, there isn't a universality. For certain things perhaps you can do it a little more readily than for others, where we know the metabolism, really the alpha to omega of the action of a carcinogen, you can be a little more secure if you know that the metabolic pathways, the dose-dependent handling of the compounds by the body, is similar in species. You can be a little more courageous in trying to extrapolate quantitative data.

But as a generalization, you are absolutely right.

Q. Applied specifically to asbestos in terms of all of the things that we have been talking about for the last day,

Q. (cont'd.) are there any kinds of issues that we have been talking about and which we can take the animal evidence that we have found and extrapolate it to humans, in any quantitative sense?

A. No, but I think that we've come back to yesterday, the point I was making - since it is relatively straightforward...not easy, but straightforward...to do body burden studies in experimental animals, and equally so in human tissues - tissues being tissues - I would have great hopes that we might be able to say that so many fibers per gram wet weight or dry weight tissue or whatever measurement you wish, might give us a basis for more precise quantitative extrapolation.

Q. We haven't got to that stage yet?

A. No, sir.

Q. Assuming mesothelioma is dose-related, is it a possibility that nonetheless it occurs at quite low doses, and indeed doses lower than you might see in the occupational environment?

A. Is it a possibility? Yes.

Q. What is there in your judgement, evidence to cast out on that possibility?

A. The fact that one can continuously, can verify the...and much point is made of it, justifiably, as one facet of the problem...the growing use and the expanding role of asbestos in the economy over the decades since World War II, let's say. I guess it's measured by the number of tons that have entered commerce and so on, and as has been pointed out in many tables and graphs, there was a sizeable increase because of the utility of the material. More than that, the material began to, within the last...well, since World War II...to get a ubiquity it did not have before...a ubiquity not limited to the workplace.

For instance, much has been made in many articles of the general population exposure incidental to the use of

A. (cont'd.) asbestos for spraying as a spray insulation in construction and so on. One read and one has had verified situations where incidental to this, material was seen around the construction site, in the construction site, floating down on Fifth Avenue or Forty-fourth Street or Madison Avenue. An awful, awful lot of people walk by Fifth Avenue or Forty-Second Street or Madison Avenue, whether it's the General Motors Building or the Chrysler Building, or what have you, so opportunities for general population exposure, the increasing use of products which again would tend to broaden the ubiquity.

One then would look, and I think...not I think, I know...the data are...perhaps Dr. Nicholson commented on this... five or six years ago we undertook an exercise jointly with the Mount Sinai group to look at possible evidence of an impact on the distribution of mesothelioma in the general population as a result of this, and we looked and we were in touch with the people who should know, and there wasn't.

So here you have a population exposed to an agent which has a marker tumor - marker as I defined it yesterday - and the failure to identify it has not been the result of oversight. There has been an alert - look for this particularly, a tumor that has generated great, great interest because of its appearance on the scene within the last two decades, and it just isn't there.

If one looks and turns to what I guess would be the Supreme Court of Pathology in the United States, the Armed Forces Institute of Pathology, and having been involved particularly in the area of mesothelioma, with the Armed Forces Institute of Pathology, one can reasonably predict what is going on in the States in the area of pathology by the pattern of consultative requests to the Armed Forces Institute of Pathology, and that has not shown a series of spikes of interest or requests on the curve in the general population situation.

In shipyard workers, yes.

A. (cont'd.) Wherever one looks, this marker tumor being sought for just has not been identified. That gives me some confidence.

And particularly I guess what brings the situation full circle is that when one looks, as many investigators have, at lungs from urban residents on a random basis, or on a stratified basis, one does find the presence of asbestos fibers, so it isn't as if they were exposed, a question...you might say well, these people were never exposed, but they have the hallmarks of having been exposed.

I think that sort of algebraically summates to a pretty strong case that at least at that dose level, you are at a level below that which is sufficient to induce mesothelioma.

Q. Let me come back to page three for just a minute. At tab twelve.

A. Yes.

Q. What do you say is the no-effect level that has been demonstrated for asbestosis?

A. Well, in the workplace I would say that the no-effect level is a combination or an end situation, is a combination of responsible speculation, in the Sir MacFarlane Burnett sense of the term, as well as data. I think that using the sources of data that we referred to before, the Weill data, the McDonald data and the like, I would say that the OSHA standard at present would appear to be...and I would have to say 'would appear to be', because it was pointed out by the Chairman yesterday that the issue of latency still is one that you cannot predict or anticipate, you just have to live with.

So I am satisfied that compliance with the OSHA standard, on the basis of available data, is a level that we would anticipate no...

Q. Two fibers?

A. Yes, sir.

Q. For both asbestosis and lung cancer?

A. I'm just talking about the workplace, and not sequestering it on the basis of disease, yes.

Q. All right. When you say you are talking about the workplace, do you include all the asbestos-related diseases?

A. Yes, sir. As of right now, yes.

Q. Including mesothelioma?

A. All of them.

Q. When you say the workplace...

A. I'm using that as the highest...

Q. All right. So that for that purpose you draw no distinction between different aspects of the asbestos industry, mining as opposed to textiles as opposed to friction materials?

A. It's the exposure in the situation that determines, and it's the body dose that is the determinant.

Q. I may not have been fair to you yesterday with Dr. McDonald, so let me be fair with you and let me give you what the testimony was that he did give to us on his own study, and let me read it to you and if you want it in front of, I'll...

A. No, I'm glad to have you read it.

Q. All right.

> This is what he says, "Our conclusion is that there is a risk, but that we can't demonstrate it, and that therefore the great importance of deciding what is the nature of the exposure-response model, and what we conclude from this, is that the exposure-response model that fits best is the linear relationship, and that therefore with a linear relationship we must assume that there is an excess mortality attributable to exposure at lower levels. I want to make that clear because it could otherwise be read to imply that there is no hazard

Q. (cont'd.) "below twenty, and the reverse is our conclusion".

Then I asked him, "So I just want to make sure that I understand that. Is what you are saying that epidemiological methods are not sensitive enough to detect the excess risk at low levels?"

He said, "Answer; That's right".

Do you quarrel with that?

A. I have no quarrel with that. That's...Dr. McDonald's coin is epidemiology the way mine is the binocular microscope, and I certainly...I would hope I have come across clearly...have infinite respect for his capability as an epidemiologist. Again, more eloquent than my saying it is my frequent reference to his work in my publication.

Q. I won't read it to you, but Dr. Weill essentially made the same point in his own article, and I take it you have no quarrel with that?

A. Not at all.

Q. One of the things that you told us yesterday, told me was, that in looking at this whole question one should look at the epidemiological data that we have. I think that's what you said?

A. Yes. I don't recall saying it, but it's a statement I could have very well made. Yes.

Q. Can you help me on this, because you obviously have a very comprehensive knowledge of all of that literature, if this Commission were going about that job - to look at that data - are there any particular studies, in your judgement, that we should give more weight to or place more reliance upon, than others?

A. I guess my..first, I'm not going to suggest the giving of weight to more than others, because I hardly set myself up as an arbiter, but if I may take advantage of the

A. (cont'd.) opening your question has given me...

Q. Sure.

A. ...it seems to me there are three or four rather key studies that may very well be enough if the elements of the study can be verified.

What I have in mind, very briefly, is the Turner and Newell study. Now that is a special resource, it is a special population, it is a special situation, and I think that...

Q. Is this Rochdale?

A. Yes. I think that were I given the responsibility, and it sounds Olympian, I apologize for that...

Q. No, I'm interested in your answer.

A. Basically, since that really represents a real situation, as indeed the McDonald and the Weill studies represent, and indeed make no mistake, the United Kingdom has grabbed this problem and attacked it a little earlier in the game than we have on this side of the Atlantic, it would be nice to really verify or get the confidence limits of the industrial hygiene measurements. It would be nice, and this I discussed with Professor Scarf who is now dead, but head of pathology at the Middlesex Hospital and former editor of the British Journal of Cancer, and spent some time at the Middlesex with him...I guess Professor Zachary has taken over since...to verify pathological diagnoses, particularly in the early days of the ascendancy of lung cancer as the most prevalent cancer in man, in males I should say, and the unfortunate proclivity of the lung as being a site for metastases from other primary sites.

Early in the game there was much confusion, because once the data were unequivocal that cigarette smoking was associated with an increased risk to lung cancer, there was a tendency on the part...and studies of data in many institutions showed that...to overdiagnose lung cancer in terms of not taking that extra step to make sure a primary wasn't there.

A. (cont'd.) So that's number one, without going into...verify the data, the raw data, from the series of studies. Not the McDonald or the Weill study, because these are studies that are sufficiently recent where the caveats were available.

I wasn't there, but I'm told how Dr. Knox and Steve Holmes, how busy they were and it was almost like in the old military days, you were given a new assignment in addition to other duties at no added expense to the government. These were the things that were done by people...these data were accumulated unlike at present, as a primary responsibility, but were done...okay, so I think that would go...

I think the same could be done in South Africa, where even though they have addressed the problem for a long period of time, the raw data...there are volumes and reams of measurements, and it may very well be that we'll find that we have to generate perhaps a lot less new knowledge than we think if these data and the sources of the data could really be reviewed.

I have found that...and just getting away from asbestos...in the years that I was the scientific director at the Cancer Institute, or Director of the Environmental Health Institute, addressing the issues where a no-go decision was made on commitment of substantial federal resources, one found that going back to the data, identifying or establishing a risk, proved to be very, very helpful.

I have specifically in mind the issue of arsenic, the issue of benzene. I guess benzene has been a matter of real concern of late, but I suspect the record would show that in the sixties I felt benzene was a human carcinogen.

Q. I defer to Mr. Warren on this topic.

A. Yes. I use this as an example. I felt that the data were sufficient despite the few cases, when one went back and documented the exposure and documented the diagnosis, and documented the specific circumstances of disease.

A. (cont'd.) So that would be my only suggestion. Let's milk all the information we have now, for all it's worth.

Q. Just to come back to my question for a minute, and I think you started to tell me, if I had to put the list together of the three or four studies that you would look at, you've told me about Rochdale, what are the other ones?

A. I look at the South African data and go through, much has been done with the populations in the mining of asbestos in South Africa.

Q. Are there any existing epidemiological studies that bring that data together, to your knowledge?

A. Oh, there have been reports at the Johannesburg conferences. I don't know of any study that brings it together.

Another crucial issue is the verification of mesothelioma incidence in Finland, the almost...the ubiquity of pleural changes in this population, and so on...terribly, terribly important.

So I would again, on Professor Merman and the others...I'm sure if one examines their data, one would come away saying that everything that can be gotten out of it can be gotten out of it, but there are lots of papers of this type.

So the Finnish data, the Italian...whereever there are occupational studies, the Bollangero population study of the chrysotile miners in Italy. There are stories, and I've spoken with members from the Pneumoconiosis Research Unit, where mesothelioma has been presumably reported in Cyprus, where it is chrysotile that is mined, not amphibole mining.

Well, I have no knowledge whether there is a single mesothelioma in Cyprus or not - other than anecdotally. I have not been to Cyprus.

Those are crucial bits of information that by

A. (cont'd.) themselves may not be terribly informative, but together they add up to a mosaic that allows you...because that's how it's done in other areas.

Q. Would all of that data be on your list?

A. Yes.

Q. In terms of the actual epidemiological cohort studies that have been done, which of those would be on your list - besides the Rochdale?

A. Oh, obviously I think you would have to begin with what you have now and work back. You would certainly have to include the Paterson, New Jersey study, and the Insulation Workers Union studies.

Q. Selikoff's?

A. Dr. Selikoff and his associates. I think that would have to be done.

I think Dr. Clark Cooper on the west coast of the United States, who has been honchoing a joint industry/ management asbestos surveillance program for almost two decades now, the data that Dr. Cooper has on prevalence and incidence of asbestos-related diseases...and I'm sure there's nothing you haven't thought of or aren't aware of firsthand, but these are the studies and what you do is you look at those. You look for consistencies and inconsistencies between these studies, and begin to try to rationalize the differences.

Q. Okay.

A. I think the Dement study requires great, great... since it really hasn't been published yet, so nobody can comment on it, it was presented at a scientific meeting...but that's the study when it is published in the scientific literature that will demand careful scrutiny.

Q. Do you have any criticisms of it, from your own knowledge of it?

A. I have some comments about it. I don't have

A. (cont'd.) them with me.

As I say, I have...it's really unfair to the investigator, and I know Dr. Dement, have for years, and I have regard for him as an individual, I have regard for the institution which just very recently granted him his doctoral degree, a very fine institution, and doctoral committee was first rate, but I am waiting for him to publish it and have it get by the editorial review board of a critical review journal, and I think that's the very least we can provide for an author.

Q. Fair enough.

A. Before you begin to look at it.

Q. The study you spoke about yesterday that your own company...which I take it is a morbidity study...the one...

A. Dr. Chase will give you the information.

Q. I know he'll give it to me. My only question is, is there a concurrent, ongoing mortality study, or is it just looking at prevalence of changes?

A. It's primarily a combination of morbidity and mortality, as I recall, and the data are being gathered in both areas.

Q. All right. Let me...

A. I had to come here to learn that Dr. Chase will be appearing before the Commission, and I said he wasn't yesterday. Obviously, I didn't know what I was talking about.

Q. Let me turn to a different topic, which is your comments yesterday on lung cancer, smoking, fibrosis.

Let me see if I can summarize some of the things you put to me, and I wrote down three propositionsthat you put to us, and let me see if I got them right.

Proposition number one: On the basis of clinical studies and animal experiments, you conclude that asbestos on its own is capable of inducing lung cancer?

A. The data are there.

Q. Fair statement?

A. Fair statement, yes.

Q. Proposition number two: Insofar as the lung is concerned, it is only rarely that asbestos is capable of inducing a neoplasm in the absence of cigarette smoking?

A. Correct.

Q. You distinguished between lung cancer and mesothelioma for that proposition?

A. Yes, sir.

Q. Proposition number three that I wrote down: If you have lung cancer in a nonsmoking asbestos worker, then the lung cancer will only be related to asbestos exposure if there is also present some fibrosis?

A. Yes, that's what I believe. Yes, sir.

Q. Let me just come back to those propositions, and let me start with the second one which is the lung cancer/ cigarette smoking proposition.

Can you tell me biologically, and I'm sure you did it yesterday and I didn't get it, but can you tell me biologically why it can happen, why asbestos exposure can produce lung cancer in the absence of cigarette smoking - why that can happen on the one hand, and yet why it is a rare phenomenon on the other - biologically?

A. Well, first, by my criteria, an asbestos-induced lung cancer would have to be...to be so regarded it would have to be anatomically located in an area of fibrosis, which would place it anatomically in the distal branches of the tracheobronchial tree, and more than that, would place it virtually exclusively in the lower lobe area adjacent to the area of fibrosis.

I find it surprising how, when I'm asked that question, people will say when have you...what made you change

A. (cont'd.) your mind about this?

I believe under tab one, there you will find on page twenty-three a human...and this was published in 1976, the paper given, I think, in 1974 or 1975...under asbestos site - lung, histology - bronchiolar.

So it's...

Q. Looking at table one now?

A. Yes. The idea that asbestos could produce a special type...special is the wrong word...a distinctive type of lung cancer, is one that has been in the scientific literature for the better part of a decade, really.

I limit an asbestos-induced cancer, noncigarette smoking associated to this, because I think the constellation of events that I described yesterday - the fibrosis, the interference with the normal viability of the epithelium, the bronchiolar epithelium, what we know historically about scar cancer, what we know about the response of this area of the lung to external irritants where epithelium will grow along the alveolar surfaces of the bronchiolar type epithelium, where it really is not normally present and so on, so yes, that is the situation of an asbestos-induced lung cancer.

Q. Why is that a rare phenomenon, because this whole constellation of events does not occur very often? Is there something biologically behind that?

A. Well, I guess it's a combination of many things. There's other pre-emptive asbestos-associated phenomenon which might preclude the development of this, the pre-emption. I don't know why it's a rare phenomenon any more than why I know angiosarcoma of the liver is a rare phenomenon in persons exposed to vinyl chloride...other than what is the focal upon which the whole thing teeters, and that is dose response.

I think we have discussed this..in fact it's in an article entitled Dose-Response Relationships.

Q. When we move from the biological evidence to the animal evidence, as I understand the animal evidence, and particularly Dr. Wagner's work, he has been able to induce lung cancer in his animals in the absence of any tobacco or cigarette smoking, quite readily.

A. Yes, sir.

Q. All right. Why shouldn't we believe the animal evidence on that issue, as it applies to humans?

A. Well, I don't know what I've said in any way challenges or generates any disbelieve in the animal evidence. I think that Dr. Wagner's position and my own are wholly compatible. There may be quantitative differences, and I think that is not unique to Dr. Wagner's work in relation to human disease, to human cancer. It's in relation to...it's common in the area you mentioned earlier this morning.

So the differences are quantitative, not qualitative.

Q. Quantitative in terms of numbers having it, or doses?

A. Well, quantitative in terms of...well, I don't see a distinction because the occurrence of one is dependent upon the other.

Q. It's the same thing. You say it happens, he says it happens, but he says it happens more often than you say it does?

A. His animals say that. I don't know how he interprets this in relation to its relevance to man quantitatively, and in fact I have an exchange of correspondence with Dr. Wagner relative to this, which happily is documentable, intimate discussions no longer ago than some four weeks ago when Dr. Wagner visited my associates and me in Denver.

I think he has been rather circumspect in avoiding any references or making any..or drawing any conclusions

A. (cont'd.) as to the significance of his animal observations to man in the quantitative sense.

I know of nothing he has ever written, and I know of nothing he has ever said, and I know very, very specifically when I asked him a question in a letter which I would be very happy to submit to the Commission, in essense some variation on:

> Chris, a regulatory agency in the U.S. is prepared to use your one-day exposure of a rat that resulted in a malignant neoplasm as the basis for promulgating some proposed rules. How useful or what do you think your data are in terms of their utility for regulation?

I know there was some variation on utter nonsense. There is no way you can use that quantitative data.

Q. He would agree with that.

A. He what?

Q. He would agree with that.

A. Yes, I think if he were to come here he would say it's...

Q. All right, let's move from the animal to the epidemiological evidence, and I know you are aware of Dr. Hammond, et al's, 1979 article in the New York Annals.

A. Yes, sir.

Q. Is that consistent or inconsistent with the proposition that you have just been advancing?

A. In terms of what, specifically?

Q. As I understand it in the famous table that several of our witnesses have put up before, the table that shows that if you've got a relative risk of one for a nonasbestos-exposed, nonsmoking population, the relative risk for nonsmoking asbestos-exposed population will be five and a fraction.

A. Four to five, or five, yes.

Q. Then the rest of equation works out.

A. Yes, well the only thing again, and this has been discussed at reasonable length with him, is what I have discussed and hopefully will get at in the not too distant future, and that is a histologic diagnosis. There are so few cancers that Dr. Selikoff has agreed to have me review the histologic diagnosis and classification of each of these neoplasms in his nonsmoking asbestos workers, where histological material is available.

You know he has two classes of information - best evidence, death certificate - and by no means does he have pathological verification. No one person has, of course.

But I would like to look at this population because it gives me an opportunity to examine the two posits, as it were, that I have made: One, the association of asbestosis or fibrosis with the neoplasm, and its anatomical site and histological relation. I think that's critical.

So I can either disagree or agree with it in terms of my coin, but certainly I have no reason to question the ability of Dr. Hammond and his associate, Dr. Seidman, to handle data correctly.

Q. But I'm...I just want to get some sense of your notion of what is rare or not rare, so I suppose the question is, if we accept for the moment...and I appreciate all the comments you've just made...but putting them aside for just a moment, if we accept hypothetically for the moment that that study accurately portrays what in fact happened, there is a fivefold increase in risk. Is that consistent or inconsistent with your proposition?

A. I'll tell you why it's an assumption...the assumption would have to include that this fivefold increase in risk is corollary to and part and parcel of the presence of

A. (cont'd.) asbestosis to a rather substantive degree to...that is the only facet I would add to my response. It would be consistent if it were associated with asbestosis to the degree that would provide this local milieu for neoplasm development, and also I would like to know what the histology of the tumor is. Histology of tumors is helpful, but really that's all it is. You really can't make any hard and fast conclusions on it, necessarily. You can in some instances.

Q. Let me ask you a slightly different question on this issue. Dr. McDonald wrote a review article, an epidemiological review article which you may or may not have seen...

A. I have not read it.

Q. He took the Hammond paper and his own work in Quebec in his most recent work, and then put forward the proposition that the relative risk of lung cancer in nonsmoking asbestos workers was at least as great as in smoking asbestos workers, although the absolute risk obviously would be much higher in smoking asbestos workers.

A. I am aware of that, yes.

Q. Do you quarrel with that proposition?

A. With his data? No. Again, I think it's a conclusion that he can only draw, he feels, from his data.

Q. And from Dr. Hammond's data?

A. Yes.

Q. Let me go to the third proposition, the asbestos..the fibrosis and the lung cancer relationship. Again, can you just help me very briefly, because again my mind may not have been working, as to why that should be biologically or medically, why there should be this relationship?

A. I'm sure I can't give you a reason why. All I can tell you is it's an observation that is decades old, that in areas of scar formation there seems to be a focus of increased risk for the development of cancer in the area of the scar.

A. (cont'd.) As I emphasize, we know so little about, really, the fundamental aspects at the tissue levels, of the origins of cancer, the pathogenesis - a fancy word that pathologists use - that I couldn't answer that.

Q. All right. What you are saying is that it's a phenomenon that you have observed, but you can't give any scientific or biological or medical explanation as to why it should be?

A. It would be so highly theoretical, that I don't think it would be all that helpful. It would involve nutritional equilibrium, availability of precursors of metabolism...I mean precursors of materials that are necessary for cell replication.

Q. Can you, on that issue, help me with a passage of yours that I don't believe I fully comprehended, and it's at your tab three. It's in the discussion after your article at page one-forty.

A. Mmm-hmmm.

Q. Someone who I don't know, but someone named Mr. Sundaram asked you two questions. Question one:

> "Do you believe that fibrogenesis or fibrosis is an essential process that has to occur as a precarcinogenic lesion before you could find cancer"?

A. That is correct.

Q. Is that what we've basically just been discussing?

A. Yes. I think Dr. Mustard asked that yesterday, and there are mesotheliomas which have been identified in the absence of any significant fibrosis, and mesotheliomas associated with large areas of fibrosis.

Q. Could you help me, the passage I didn't understand was your answer to that question, which appears at the top of page one-forty-one, where you say:

Q. (cont'd.) "For the first question, I would have to give you two answers. Fibrogenesis as a pathogenetic prelude to bronchogenic carcinoma, certainly not as a temporal prelude, yes."

A. What I meant was that you have to have the fibrosis...which is consistent with what I have been saying...you have to have the fibrosis beforehand, which leads to the local situation that gives the cancer.

As a pathogenetic prelude, obviously not because it isn't a fibrous neoplasm that you are getting, it's an epithelial neoplasm.

Do I make myself clear?

Q. I think so.

A. Basically what I'm saying is that you have to have the fibrosis to create the local environment for the development of the cancer. But it is not the fibrous tissue that gives rise....the cells of the fibrous tissue are not the cells of origin of the cancer, it is the epithelial tissue that is. So that pathogenetically it is not the prelude to the cancer.

Is it clear now, I hope?

Q. Yes.

A. Thank God. I guess when you answer questions you don't have the opportunity to rewrite and above all have as literate an associate as I have to make things clearly intelligible.

Q. Then when you talk about mesothelioma, is your answer different on the question as to whether there has to be some antecedent fibrosis?

A. No. I would say that it can or cannot. Yesterday I pointed out that there are data from...I think it's an issue that isn't yet resolved in man.

Q. Is there any epidemiological evidence of which you are aware that supports the relationship between fibrosis and

Q. (cont'd.) lung cancer?

A. No, I think...fibrosis and lung cancer?

Q. Yes. The antecedent evidence of fibrosis before you get lung cancer?

A. Oh, I think ...again it may very well be anecdotal...but in the Rochdale study, I recall discussing with Richard Doll, and perhaps with Dr. Lewinshohn, I'm not sure...but they felt that where they did have pathological material, it was invariably present.

In fact, I think it was fair to say that the position at that time of the British pathological community was that they felt the presence of asbestosis would be necessary to identify or catalogue a tumor as an asbestos-induced lung cancer.

I can't say whether they hold that position now or not. You are going to be in a position to find that out very shortly.

Q. Is there any other evidence?

A. Again, the evidence is a reflection of the scientific principles you bring to...yes, there's evidence because from that point of view, I say it's evidence.

Q. All right.

A. I could be as wrong as the very devil, but...

Q. When you look at the question of compensation and attributability, do you apply that principle that you have just been talking about to determine whether you are going to compensate for lung cancer in terms of whether it's asbestos-related? Is that the principle that you would apply?

A. Yes, I would apply the principle of somebody having some asbestosis, and bronchogenic carcinoma, as having qualified for compensation.

Q. Is there any magical level of fibrosis that's necessary?

A. No, you see, there's an art and a science to

A. (cont'd.) everything you do. My mentors, I never could understand how Professor Saffear or Professor Steiner or Professor Stewart could really look at a slide and say 'this is what it is', and three hours later I would still be looking, as a resident, trying to see what they saw in three seconds.

There is a feeling I have, and it's not unique to me, it is how pathologists work. There is an impression you get, and this is why experience is so crucial. It's how much you see, how vast your experience is, that gives you, that summates to what we commonly call expertise.

Q. Can I turn for just a moment to gastrointestinal cancer, and I'm not certain I know what your position is on that.

Do you say it can be caused by asbestos exposure?

A. I have serious doubts. And again, one has... what one really has to be very, very careful in taking a firm position where there are contradictory data, but what I think I can do is articulate a position I have taken as long ago as a decade.

Q. Sure.

A. That is, first of all the assumption that... gastrointestinal cancer really turns me off as a term, in the sense that the epidemiologic associations with the various levels of gastrointestinal cancer, long before we even think of asbestos, are different. You have the upper gastrointestinal tract, the oral-facial area associated with malnutrition, alcoholism, the susceptibility associated with rather severe vitamin deficiency. There is the association of esophageal cancer with certain syndromes in Scandinavia, alcohol ingestion, it has been identified with.

In the Transkye area of South Africa, it's an epidemic cancer for reasons that we really don't understand.

Gastric cancer is a law unto itself in the

A. (cont'd.) anthropologists' sense of the term. It's a disappearing disease in the western world, in the areas of high endemicity it is still high and actually increasing. There are data in pockets of the world which show anatomical, histological changes that appear to be related to high susceptibility.

Small intestinal cancer is hens' teeth, I think, the saying you give to sophomore medical students. Colon cancer is yet a different disease in terms of its epidemiological patterns, and rectal cancer is different than the colon again. The relationship of certain types of congenital benign tumors or premalignant tumors, if you want to call them, are determined.

So while the only...well, clearly physiologically it's the gastrointestinal tract. Histopathologically, histogenetically, and particularly in response to external agents, it differs.

So I think gastrointestinal cancer can be misleading when it's used as a generic term, as it were. But nevertheless, there are data which show a risk...not of the magnitude of lung cancer, but nevertheless a risk that will chi square out to a P value that the statisticians denotes statistical significance.

One would have hoped...and in two studies...well, as I say, one would have hoped that in gastrointestinal cancers associated with asbestos occupational exposure that some stigma of asbestos effect on the nonneoplastic side would have become evident.

What do I mean? When Dr. John Berg, who was then at the National Cancer Institute and then moved to the University of Iowa, did studies on a series of cancers of the colon submitted to him by the Mount Sinai group for not only histological evaluation, but electron microscopic study...like microscopic studies for the presence of fibers, and so on... evidence of fibrosis and so on, he was unable to find it.

Indeed, in experimental studies where asbestos

A. (cont'd.) has been fed, the fibrogenic capability has not been demonstrated.

Feeding studies that have been done have been uniformly nonproductive of neoplasms, but that just means in that experimental milieu you can't have it both ways. I don't know how much you can extrapolate from those.

But nevertheless, I have said and continue to say that it would be nice to examine the histology of the cancers to see what is...and gastrointestinal cancer, like lung cancer, has been studied to a faretheewell...part of my training with a man by the name of Steiner who classified stomach cancers until hell wouldn't have them...and really, they all had different natural histories, they all had different patterns of development.

I don't know. I would say that, using the same reasoning I did yesterday, that the summation of all the data, the statistically significant in some and nonidentification of an increase in others, what we know about the histogenesis and the pathogenesis of gastrointestinal cancer at its various levels, and the really...the epidemiological data, again in the studies of the Mount Sinai group or the studies in Canada...are either best evidence or death certificate. Maybe it's just the tubular vision of my being a pathologist.

I would like to see...and not because there's anything hallowed or sanctified about pathology...but the histology can tell you so much. It really can be terribly informative, and again I've asked in discussions with the Mount Sinai group, with the wisdom, and Dr. Suzuki, the pathologist of that group, what their ideas would be about the wisdom of just looking at these tumors histologically.

In summation, I don't think the evidence is convincing that there is an increased risk to gastrointestinal cancer that can be attributed to asbestos exposure.

Am I saying that the statistical data showing it are wrong? No. All I'm saying is that it's equivocal.

Q. It's equivocal?

A. It's equivocal, yes. But certainly a fast yes and a hard no are, at this stage, premature. I believe the answer is no.

MR. LASKIN: I believe Dr. Uffen had a question.

DR. UFFEN: I suspect now that it is trivial, but it's a translation into lay language. What is meant by pharyngeal transpassage from the trachea?

Does that mean swallowing?

THE WITNESS: Exactly. Exactly. I guess I was being paid by the word, or something.

What it is is an attempt to show, in that same phrase, show where the stuff you are swallowing comes from.

MR. LASKIN: Q. Just lastly on this series of questions, what is your judgement on any relationship between asbestos exposure and cancer of the larynx?

THE WITNESS: A. There again, you have the confounding factor of the high association with cigarette smoking, and you have studies which purport to show an association, and studies which do not. Here I don't think I necessarily take or feel that histology or pathology is going to make all that difference in arriving at a conclusion. I think there should be some more studies to resolve this difference.

The literature contains evidence and conclusions of an association - I think Dr. Newhouse, and certainly Dr. McDonald, did not see any.

Q. Would you be looking for, again, antecedent evidence of fibrosis?

A. Certainly antecedent evidence of fibrosis would be important to me in terms of thinking a second and third time about a role for asbestos.

Q. What about with respect to gastrointestinal

Q. (cont'd.) cancer...I didn't ask you that... would you also be looking for antecedent evidence of fibrosis?

A. Yes, because that would be a marker to me of exposure sufficient to induce fibrosis, and then I would look at the data for any one case. You know, you can't say, but from an epidemiological point of view I think that would be worth knowing and important to have.

Q. Can I turn just very briefly to another topic, and that is your discussion yesterday about fiber dimensions and relative hazardness of fiber dimensions and the actual measurement of fibers. What I want to do is try and relate your testimony yesterday to what we can see and what we can't see under the optical microscope.

Let me just put two propositions forward. One is the obvious, and that is that under the optical microscope we measure and define only fibers greater than five microns in length with at least a three-to-one aspect ratio. All right, point one.

Point two, we have had expert evidence which would suggest that because the optical microscope only has a certain resolution power that even if you've got a fiber, say ten microns in length, if it's got a diameter less than point two, you won't see it under the optical microscope?

A. This is what the experts say.

Q. Taking that framework and applying it to what you said yesterday, relatively speaking should we be worrying about the fibers that are smaller than five microns in length?

A. Relatively speaking I think we shouldn't in the sense of the experimental data that are available, and the fact that there, at least, there is a consistency. I'm just using...having done no measurement myself and not being an expert in measurement...

Q. But on the basis of your understanding of the

Q. (cont'd.) experimental evidence, on a scale of relative hazards, the fact that we don't see the fibers smaller than five microns in length under the optical microscope is not a great cause for concern?

A. On the basis of the described pathogenecity, I would agree with that.

Q. Do we have to worry about the fibers greater than five microns in length that we can't see because they are too thin, under the optical microscope?

A. There I think you have to be concerned because of the forked-end fibers. I think yesterday there was ample evidence that, as we have discussed, that supports the concept of thinness being a factor.

It's very interesting that...the only comment I would make is, one would be well advised to, again, knowing the physiology of transport of particles through the respiratory tract, the concept of suspension in tidal air or the concept of very, very thin fibers being more amenable to dissolution, handling within the body, and of course I guess that theoretical concept really was a theoretical concept until one bit of data came along which I think surprisingly, but rather precisely, demonstrated this in an experimental model...not with asbestos, but with manmade vitreous fibers, where doctors Kushner and Wright did some intertracheal installations and they demonstrated that indeed the long, thin dogma...if that's what it is...was entirely compatible with their results. But they found a biphasic response - as you got thinner, you increased pathogenecity to a point, and I don't remember, I don't have the article in front of me, but there was a point of thinness beyond which there was a disappearance of pathogenecity. Since these were two sort of universally recognized as careful and meticulous workers, I think that really does give a little more... it doesn't prove anything...but a little more substance to the

A. (cont'd.) concept that there is a point of thinness where the potential pathogenecity is compensated for by the ability of the body to get rid of the stuff pretty rapidly, or it just doesn't get settled out.

Q. Could I go briefly to your statement to the House of Representatives, looking at education, which is at tab seven?

A. Yes.

Q. Can I take you to the last sentence on page one, which goes over to the top of page two?

A. Yes.

Q. I wonder how far you would take that statement, and for example, do you take it so far as to say that if there is asbestos in a school, that is loose or friable, that you can leave it there with no risk to health?

A. No. I take it only as far as dose response will let me take it. Clearly, there are circumstances where the dose response associated with the deliberate, or with circumstantial, I don't mean deliberate, but where circumstances can clearly create exposures at unacceptable levels, above compliance levels, obviously the hazard is there.

What I meant was that, as it was there, the discussion was related to the material that was there by virtue of its having been applied that way, not by virtue of anything that might have been done to it since then.

I think that's rather clearly borne out in the give and take of the discussion, and the question and answer period with members of the subcommittee.

Q. When you talk about dose and dose response, and you've got a discussion about low doses on page four, in terms of everything you talked about yesterday, in terms of defence mechanisms and so on, is there a difference biologically in the way in which one gets the dose? For example, does it matter to

Q. (cont'd.) the whole defence mechanism, clearance system, that you talked about as to whether you get a certain amount of dose in a short period of time as opposed to that same dose spread over a longer period of time?

A. It varies with the agent, but clearly it does because one of the things that we discussed yesterday was the finiteness of all the defence mechanisms. So that...

Q. What about with respect to asbestos?

A. The same. I mean, that has a finite...yes, it has been known...again, one of the principles of carginogenesis, for reasons that one can't go into right now, but one of the universally recognized principles is the fact that a dose, a hundred units of whatever it is, given at one time will behave differently than that same hundred given in doses of ten units at intervals.

Now, it may vary from agent to agent, depending upon how the agent is handled biologically. In some cases it is dissipated.

But clearly there is a difference between a series of high spurts, pulses of exposure, as it were, as distinguished...

Q. Applying that difference to asbestos, what is the difference?

A. The same as it would be, that basically if exposure is at a level which is consistent with maintaining a physiological state of activity for the defence mechanism, you are presumably at less risk than overwhelming the defence capabilities.

Q. You refer on page four to two studies to support your argument, and one I think I know about, it's the study by Dr. Selikoff, I take it, in the area surrounding Paterson. I think it was Riverside and one other community.

A. That was one that was reported at the New York Academy that you referred to. Exactly.

Q. The other one I don't think I know about, is the roofing worker population.

A. It has been published in the New York Academy, oh, 1972, maybe, 1973. I can't remember.

But what Dr. Selikoff and Dr. Hammond did was identify a population of roofing workers, members of the Roofing Workers Union, and very ingeniously said we can study two or three things simultaneously: first, these are people who are exposed to coal tar and its derivatives, with its carcinogenic polycyclic aromatic hydrocarbons; two, this is applied to asbestos-contained materials for built-up roofing, the layer of tar, the layer of paper; and third, it was an outdoor population which they felt would give them some additional information in terms of no restrictions on smoking, as there is in some areas.

What they felt was that they had the mesothelioma as the marker, lung cancer as a target for both the carcinogenic polycyclic hydrocarbons present in the tar, and the lung cancer associated with cigarette smoking. And in a study that was designed no differently than are other studies, they indeed found an increased risk to lung cancer which was the formulae that Dr. Hammond has...he felt he had demonstrated...was due to the cigarette smoking, coal tar...at least he ascribed that, but they didn't find a single case of mesothelioma.

The absence of this marker convinced them that even though there was measurable asbestos and they didn't do a comprehensive industrial study, but they did make some measurements to see whether indeed there was some asbestos associated with the occupational exposure.

So that's the story there, and this was published... you would probably not recognize the content by the title, but I think the title of the article is, I think it even has hydrocarbon in the title, and if this were not a presentation to a

A. (cont'd.) nonscientific group, it would have had a bibliographic reference. It's one that you can easily come by. A phone call to Mount Sinai - send us a reprint of your roofing paper.

Q. Thanks Dr. Kotin. You've been extremely patient with me, and I'm going to turn you over to my colleagues.

DR. DUPRE: Thank you, counsel.

Just before I invite the first counsel to cross-examine, is your maintenance person still expected?

(REPORTER'S NOTE: Inaudible discussion re maintenance.)

DR. DUPRE: I was just wondering, would you like a cup of coffee at this point, Dr. Kotin?

THE WITNESS: I would like one, yes. Thank you.

DR. DUPRE: Why don't we break until ten to ten.

THE INQUIRY RECESSED

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THE INQUIRY RESUMED

DR. DUPRE: Are we ready?

MR. LASKIN: Yes.

DR. DUPRE: Mr. McNamee, do you wish to go first?

MR. McNAMEE: Yes, Mr. Chairman.

DR. DUPRE: Proceed, please, counsel.

CROSS-EXAMINATION BY MR. McNAMEE

Q. One of the questions Mr. Laskin asked had to do with the use of asbestos in schools, and I don't know whether he covered it, but you used the term in that article that a representative 'inappropriate' use of asbestos. Did you mean...?

A. At the time, I guess, I wasn't there when decisions were made, but retrospectively it would appear that from the point of view of its utility it is obviously very appropriate,

A. (cont'd.) but from the point of view of the natural history of what has happened since then in terms of pictures you see where kids make a special point of trying to do things to it, and so on and so forth. This is what I meant.

Q. So from a practical point of view, it did have utility? It did the job?

A. Oh, I'm sure that it served a very, very useful purpose and this is why it was done.

Q. In Mr. McKinney's testimony before the Congressional Committee, I think it's tab six, page 519, I think we found out an answer to the question Miss Jolley asked one of the previous witnesses about injection of asbestos into the lungs of human animals.

This had to do with the injection of the lungs and the pleural cavities of submariners in the Second World War?

A. Yes.

Q. Did anybody follow those people up and find out what happened to them?

A. There is no way I can go into, in less than an hour, telling you the actual efforts we have made to follow that population up.

From St. Alban's Hospital, the naval hospital where this technique was used, to the National Naval Medical Center, to the repository of all veterans' records in St. Louis, to the submarine command, my meeting with the Chief of Naval Operations and the Surgeon General of the Navy, and then having, just strangely enough, Dr. Sawyer who has been involved, as you may know, remember the name from the issues of asbestos in public buildings and so, was a submarine medical officer and he used his contacts...well, we got a series of promises. But basically, that population which had had this surgical intervention has still escaped analysis. We know where a sporadic case is here and a sporadic case there.

There was a big fire in the Veteran Administration

A. (cont'd.) Record Repository in St. Louis. At one time we heard that these were part of the records that were destroyed then. I don't know.

Q. Well, with whatever followup you've done, have any cases of, say, mesothelioma been encountered in this cohort?

A. No. The only case there is is where, in the literature, there is a case where asbestos was put into a pericardial cage, pericardial sac, for much the same reason, to establish fibrosis in circulation, and there Drs. Churg and Howell have reported a case of mesothelioma.

Q. The one thing that would be known, of course, is the amount of dose that was given?

A. That's correct.

Q. Was it a massive dose, or just a minimum dose?

A. It was a...it really wasn't pure asbestos in most cases. What it was was a talc containing asbestos fibers. It was a tremolitic asbestiform talc that was used.

Q. Dr. Acheson, who testified a few days ago, in one of his papers, tab number three, he described...it's called Mesothelioma in Exposure to Mixtures of Chrysotile and Amphibole Asbestos..and appeared in volume thirty-four, number four or Archives of Environmental Health. It has to do with the analysis of tissue specimens of lung cancer and mesothelioma victims, and you, yourself, as a pathologist...well, basically you analyze the fiber content, obtain a fiber profile.

A. Yes.

Q. Are you aware of this study?

A. Yes.

Q. You, yourself, have you done any fiber profiles of mesothelioma?

A. None. No, sir. I have done none.

Q. But are you aware of any other studies aside from this?

A. Yes. Drs. Timbrell and Pooley at Cardiff are doing studies. Professor Vigneau in France is doing studies of this type. I think that at Mount Sinai, Dr. Langer and Dr. Rowe are engaged in studies of this type as well.

Q. As a layman having heard that evidence and reading it, it seemed to me that there is a fairly powerful indictment of crocidolite, if you take these results...

A. It is certainly...the data are there and that is why in my testimony yesterday I certainly didn't reject the possibility of crocidolite. It's just that at this stage of the game a little more information like that could make an overwhelming difference in my position.

It certainly is in the area that I said is going to make the ultimate determination whether...not necessarily what I think is important, but from the point of view of the acceptability by the scientific community around the world, it's this type of study that is going to do it.

Q. Dr. Acheson indicated that maybe he is in sympathy with you on this basis, that fiber-for-fiber one asbestos type is as carcinogenic as the other. He said that maybe with crocidolite the dust cloud is the...it takes less energy to raise a dangerous dust cloud. Is this in line with your thinking?

A. Yes. That I am in full agreement with.

Q. You have indicated that the mechanics for engineering of how the fiber particles, asbestos fiber particles reach the pleura is not known, or at least there are theories, but not...is this partially...and it may be a facetious question... is this something that hydraulic engineers or physicists might aid? They might know as much about that as a doctor?

A. They wouldn't know as much, they would know a lot more, because certainly...this is not my field...but certainly in the area of cardiovascular disease the engineering

A. (cont'd.) principles of rheology have great application to the study of cardiovascular disease, and surely the forces are there and with the new techniques, the recent techniques...recent, I'm talking a couple of decades...of isotopically labelling materials, the bioengineering capabilities of simulating lungs...I don't know whether you are aware, you probably are...that actually there are mechanical lungs which for all intents and purposes, from the viewpoint of physics, are really elegant models of the dynamics of respiration, and these are things made out of manmade materials.

Q. Yes, and what about...you are talking about these tracer materials and I was thinking, say with monkeys, I would assume the pathogenesis of their mesotheliomas are somewhat like humans' mesotheliomas...could not these trace elements be put in with asbestos and with x-ray, periodic x-rays to see how they disburse or go to the pleural lining?

A. They could, and I'm really not aware of the latest work going on at the South African Institute for Cancer Research, but certainly they are using the baboon population they have for bioassay studies, as well as for studies on mechanism.

I rather suspect, though I can't absolutely state with certainty, that they are studying translocation in nonhuman primates as well. Certainly, nonhuman primates have been used and are very, very useful for studies of this kind.

Q. In these...like Dr. Acheson's analysis of Dr. Pooley's data, we understand that asbestos fibers do reach the pleural area. What about some of the other particles that are in the lung, that are inhaled. Do they also have this quality of being transported to the pleurae, or is it a special attribute of an asbestos fiber?

A. No, it's..any particle can be transported to the pleurae, and in fact it's not uncommon in an autopsy, life

A. (cont'd.) experience, to see red lungs in cases of siderosis, or black lungs in the case of coal workers pneumoconiosis, or the residents of Pittsburgh or St. Louis in the old days.

No, the particles can get out to the pleurae as well. Yes, sir.

Q. As I understood your evidence, you more or less restrict the carcinogenic fibers to a certain size...at least within a range. Is that correct?

A. That's correct.

Q. When Dr. Berry was here, I think he testified as to an ulcer in his article, tab number three, about very fine grinding of asbestos fibers down to superfine sample number seven fiber. I don't know what that is, but I gather it's pretty small. Is that a fraction of a micron?

A. It can be ground very...yes. It can be ground to virtually any predetermined dimension that you wish.

Q. Would this number seven be a smaller size than the fiber type we are talking about?

A. I would have to see just what he is referring to, because there is a commercial method of rating asbestos which has to do with fiber length and quality. That has numbers as well.

Q. Whatever this number seven was, he indicated that in a rat population it produced a sixty-six percent mesothelioma rate in one of Berry's studies in 1969, and I didn't know myself whether he was talking about a...

A. He was talking about a long fiber, a long, thin fiber there.

Q. Even when it's ground down, it's still long and thin?

A. As I say, you can grind it any dimensions you wish, and I just don't know. I would have to recall...

Q. That wasn't clear to me whether this was grinding down way below the acceptable range of size.

A. I can't answer that. I know the article, but I don't recall the actual...

Q. You have indicated that a physical change might affect a carcinogenic property of a mineral or a substance, is that correct?

A. Yes, sir.

Q. You gave the example of drilling holes in a dime.

A. Or a piece of teflon or plastic.

Q. Would such a simple operation as, say, bending it, bending the dime, be a physical change or not?

A. I don't know that that has been done.

Let me just take about thirty seconds to show you what actually has been done.

This represents a film, anything from the size of a dime or smaller, round, and you implant that, and you get your malignant neoplasm. If you drill holes in this and then reimplant it...not the same one, but drill holes in exactly the same thing and implant it...you don't get any tumors.

In fact, the assumption was that these holes reduce the number of cells that were immediately apposed to the carcinogenic stimulus, and therefore with fewer cells at risk you didn't get any tumors.

What has been done is, you take a big thing and drill holes in it. Well this, even with the holes drilled, has a surface area a multiple of that, but it still applies.

Then the same thing as I say applies in relation to size when I was talking about big granule, smaller granule, the powder, the dust and even the mist, and so on, so that alteration of the type that you mentioned, spatial alteration, probably would make a difference. Nobody has done it, because in

A. (cont'd.) addition to the molecular and physical structure of a compound, one of the things that relates to a compound carcinogenicity is its steric properties, its three-dimensional properties. So that you can take a known potent carcinogen like a polycyclic aromatic hydrocarbon, benzpyrene, or you can take an aromatic amine like dimocetaminofluorene, a dye, and you can substitute a molecule of...one molecule for another...I mean one atom for another in this molecule, and alter its steric properties even though you have minimally, virtually not at all, altered its chemical properties, and enhance carcinogenicity in some instances and obliterate carcinogenicity. So that carcinogenicity is the sum total of chemistry, physics and dimensions and steric properties, varying all over the lot.

MR. McNAMEE: Dr. Uffen wants to ask a question.

DR. UFFEN: Could I ask a question here? I think it sort of fits in here perhaps better than some other time.

When we are talking about the hydrodynamic properties of fluids in passages like biological engineering, we try to observe the principles of dimensional similarity, similar to, or scale modelling. If you scale down in size, you have to be very careful that you scale down properties also.

Now, in fluid dynamics we pretty well know how to do that now by use of things like the Reynold's number. What I'm curious about is when you move to an animal, where you scale down the size of the biological system, is there any analogous principle of similitude that must be observed?

THE WITNESS: No. It would be nice if we had something like that, but the response of a population of cells is completely unpredictable because the population of cells, as I think about it, it would almost be impossible to get an equivalent number in the field of carcinogenesis, because not all the cells in a given cell population exposed to a carcinogen are in the appropriate phase of cell division to be responsive

THE WITNESS: (cont'd.) to a carcinogen.

A carcinogen will be active on a cell during its, during one phase of its reproductive cycle, during its phase of mytosis, and the cells in any given tissue or organ do not... are not synchronous. Cells are dividing at different rates and in different patterns normally. In experimental models you can produce cell systems that divide in synchrony, but the normal tissue does not have a synchronous division of cells.

DR. UFFEN: Can you tell the difference between the cell from a specific part of the lung of a small mouse, and a human, and an elephant?

THE WITNESS: No, sir. No, sir.

MR. McNAMEE: Q. Well, just to go back to the punching the holes, that might have something to do...to my uneducated mind...something to do with these principles of macrophage and being able to surround and attack, because you've got that many more openings. Where maybe if you, say, take another and just feather the edges or made it star-shaped, it might not do anything. It's still the same bulk.

THE WITNESS: A. It could. Really, again, there are two explanations for these, both of which I think are of use in discussing the process and our understanding at this stage of the game.

Q. With respect to the mesothelioma cases, are all these cells the mesothelium in the peritoneal area and also in the pleural areas, the same type of cells, or is there some differentiation between that and...

A. Oh, no. It's the unusual mesothelioma that has a homogeneous cell population. In fact...in other words, where all the cells look alike like a starry sky, or something like that...in fact, one of the most common form of mesothelioma is one which has what we call a biphasic pattern. One type of histological geography at one part of the tumor, and a different

A. (cont'd.) type in another, and in a third place they are intermixed side by each, and so on.

It's unusual for cancers to have...

Q. I think I obviously misphrased the question. I mean the mesothelium cells themselves, not the cancerous cells, but the lining?

A. They are similar.

Q. Are they also similar to the lining that you are talking about in the bronchotrachial tree?

A. No, they are different. They have a different function. The function of the lining, of the mesothelial cells, is to provide a silicone-like surface, I guess, would be stretching it, but nevertheless, normally during inspiration and expiration it would not be uncommon sometimes for the lung surface to appose and hit the chest wall surface...certainly the intestines bounce and move within the abdominal cavity...against the walls of the abdominal cavity, and the interesting is that to keep them from adhering to one another, to keep adhesions from forming, they have to have a silicone-like surface that will allow them to bump against each other and still produce no reaction, and therefore not stimulate the formation of fibrous tissue, which in that case would be an adhesion.

Q. With respect to asbestosis, I think most of the evidence indicates that primary site is the lower lobes of the lung. Is that more or less true with pleural mesothelioma, too?

A. No, they are observed all over...predominantly the lower chest, but they are seen all over. It doesn't have the consistency that asbestosis has for the lower peripheral area.

Q. You have indicated that the dynamics of how the fiber reaches the pleural area are not clearly known. Is it possible that obviously these, whatever method the fibers

Q. (cont'd.) take to get to the pleural area, they go through this...they have already gone through this clearance procedure you are talking about, the mucociliary apparatus? They don't bypass it?

A. Some have, some haven't. No, they all have come in through...you are right...through the tracheobronchial tree. Sure.

Q. Can those...is it possible for those fibers to be passed through the walls of the lung and into the stomach, or is there just too many barriers to that...to cause peritoneal cancer?

A. Oh, no. No. Let me divide your question into two parts, if I may. Is it possible for fibers to penetrate the intestinal wall or the stomach wall? Yes, it is. Whether this is a mechanism for the formation of mesothelioma, I don't think anybody knows. There are opinions that it's the passage through the lymphatics from the lung, from the chest cavity through the diaphragm into the abdomen. So the issue of the actual evolution of an abdominal mesothelioma is still a matter of debate.

Q. In extensive autopsy, would any of the other organs be examined to see whether...for the passage of asbestos fibers through them?

A. Well, not as part of a routine autopsy, but where you have a specific research program going on or you have a specific reason for looking at them...as I mentioned before, where tissues from asbestos workers with abdominal mesotheliomas, with abdominal gastrointestinal cancer, have had their special pathological studies made of the tumors as well as the intestinal tract, but that would only be a very special study requiring a nonroutine...the use of nonroutine methods for analysis and study.

Q. Just one further area of questioning. You have indicated that one of the reasons why smoking is connected with certain asbestos-related disease is that it knocks out these

Q. (cont'd.) two defence mechanisms, basically?

A. Yes, sir.

Q. So, say two people exposed to a heavy dose, one a smoker, he is going to have a maybe fifty or seventy-five percent of his defence mechanisms at least impaired, and this is going to cause the increased incidence of cancer?

A. I believe that.

Q. Assuming that these fibers, say in the nonsmoker, they pass through these two defence mechanisms and then they are deposited on the pleurae, for some reason I would...in my layman's mind..it would seem to me that a smoker might also, because his defence mechanisms have been knocked out, he would be more subject to mesothelioma than a nonsmoker. From that I somehow think that there may be other factors, aside from fiber size, that might have a...

A. That could very well be. We just don't know that much about it, other than the fact that what we do know about differences in latent period, I think, a consistent observation in most epidemiologic studies has been a longer latent period for mesothelioma appearance than for lung cancer appearance, and it may very well be that the mesothelioma, any smoking influence on mesothelioma is masked or pre-empted by that lung cancer that comes along earlier...due to the shorter latent period.

That's just speculation, I don't know. But I think what I say comports with at least the theoretical knowledge that we have.

MR. McNAMEE: I have no further questions. Thank you Dr. Kotin.

DR. DUPRE: Thank you, counsel.

Next?

CROSS-EXAMINATION BY MS. JOLLEY

Q. Dr. Kotin, the first line of questioning I would like to pursue is the defence mechanisms, because we went...

Q. (cont'd.) Mr. Warren took you and us through a very elaborate description which lends itself to animation of legions of macrophages and fibers fighting out, etc., and ciliated mucous escalators, that kind of thing.

I mean, I think we are all constantly impressed by the capacity of the body to help itself in defence against things.

You mentioned that Arthur Morgan in fact predicted that ninety-five to ninety-nine percent of the fibers would perhaps be cleared in a healthy individual, a nonsmoking, healthy asbestos worker?

A. Well, I think this is in the literature. I think Dr. Becklake has published that.

Q. Right. She mentioned ninety-eight percent in her...right.

A. Yes.

Q. It's the same reference then.

That's fairly impressive and it gives you a sense that, you know, that's...but I wonder if we could talk about actual fibers in the workplace and I wonder what do you consider...this is probably an unfair question...but do you think that two fibers per cubic centimeter is an acceptable workplace level?

A. On the basis of existing data, yes.

Q. Let's take the two fibers of more than five microns, per cubic centimeter, over an eight hour day. A worker breathing in that, without a respirator because we presume it's safe, and over an hour an average worker would breathe in a million cubic centimeters of air.

A. That's about right.

Q. Is that correct? And over eight hours, therefore, taking two fibers for every cubic centimeter...and presumably, that's probably exaggerating, you are getting

Q. (cont'd.) approximately sixteen million fibers per cubic centimeter?

A. Yes.

Q. I mean sixteen million fibers of more than five microns in length, entering the lungs?

A. Right.

Q. Well, perhaps not entering the lungs, but...

A. But entering the tracheobronchial system.

Q. Let's take the ninety-nine percent, because this individual is very healthy, and presumably ninety-nine percent of those fibers are being exhaled or gotten rid of in one sense or the other. One percent of sixteen million fibers leaves you with a hundred and sixty thousand fibers left in your lungs after one day of exposure at that level, and I find it very hard to believe that a hundred and sixty thousand fibers is a no-effect level.

A. I have no way of responding to that. If you find it hard to believe, I respect your disbelief.

Q. I mean, that's only one day and these workers work for more than one day in asbestos fibers.

I would like to pursue the no-effect level, if it's all right with you, and that is that it seems to me when we went through your biography yesterday...you certainly had a very impressive biography....and with a lot of public health agencies, and my understanding is that in 1973 you testified as a witness on behalf of the Office of Hazardous Materials Control for the United States Environmental Protection Agency. Is that correct?

A. That's correct.

Q. I think you could testify for a number of agencies as a public health official.

In 1973, in November...that was the testimony... you indicated that in fact there was a no-safe-threshold for asbestos?

A. I was speaking as I spoke yesterday, of the molecular interaction. One molecule can react with one element in the DNA, and clearly how can there be a threshold if that is for the transformation of the cells. It is the promotion and the other factors for which there's a series of thresholds, and I can tell you that in 1970, before that, I was a member of a certain group where I said exactly the same thing, as part of an expert group appointed by the secretary of HEW. There are no inconsistencies between my position then and now, on the basis of both the intent of the information then and the subsequent information, in terms of the vast knowledge of DNA repair which has entered the literature in the last five to ten years, and the monumental work done not very far from here by Dr. Farber and his associates here, and Dr. Peto and his associates, on the stepwise sequence associated with carcinogenesis and the threshold...to use the word...bases for effect or no effect.

Q. In one of your testimony as well, you presented apprehension about one fiber per cubic centimeter and the fact that you felt there perhaps was risk involved at one fiber?

A. I don't recall that.

Q. That was in an ABC interview with you two years ago.

A. Well, the ABC interview was Mr. Bergman at, I guess Upton Sinclair put it best...in the best brass check aspect of journalism. That has been repudiated even by ABC, that program.

Q. Could I take you back to yesterday's testimony, and that is that you were talking and I understand Dr. Chase was going to present this material to us, but we were talking about no-effect levels for carcinogens, and all of a sudden you described to us your modern plant as an indication of a no-effect

Q. (cont'd.) level. My understanding is your marker disease there was asbestosis, is that correct?

A. We are in the process of getting the others as well, and all I reported was asbestosis. But as of right now, we have had no indication of any neoplastic disease as well, it's just that the data have not been accumulated and presented in the tabular form which will warrant its scrutiny.

I might suggest that the data which we have, there is no way to have the validity of your data checked than by having people who have extensive experience in the field, and I believe it was, what, three weeks ago, Dr. Chase? ...that Dr. Chase and I, data in hand, flew to New York and had Dr. Nicholson and Dr. Selikoff, in the course of a whole day, review the data from the point of view of clearly getting the added benefit of their experience, and also having them see things that perhaps we didn't see.

So the data are there for presentation. They will be presented, and we look forward to having both its merits and its shortcomings pointed out to us.

Q. I would like to move on to smoking cessation programs, and that is that you made some very strong statements yesterday and you have always made very strong statements about smoking and the implications of smoking and asbestos, and that smoking cessation programs are very important.

I think you would agree that asbestos workers would obviously reduce their risk if they stopped smoking? I mean, that's the premise on which your...

A. Yes. When we started the program, the risk was limited to lung cancer. But now the most recent report of Dr. Selikoff to the National Institute of Environmental Health Sciences clearly moves smoking from the category of aggravating asbestosis, to now having a demonstrable and verifiable role in increasing susceptibility...as it has for lung cancer, though not to the magnitude.

A. (cont'd.) So perhaps for even more reasons than we initiated the program, there exists now.

Q. I guess I would like to talk a little bit about corporate responsibility, because one of your papers that was presented to us was...I think it was tab number two...was called The Industrial Medical Officer and Corporate Responsibility.

A. I know the paper.

Q. Given that obviously lives would be saved if asbestos workers and former asbestos workers stopped smoking, and the fact that corporations know about that, and I think that has implications for punitive damages in lawsuits, certainly in the U.S...

A. I have my M.D., not my LL.B.

Q. Neither do I, so...okay, as a public health matter then, do you think it should be a corporate policy for every company involved in the asbestos industry that they should notify every worker or former worker of the risk involved in smoking and asbestos?

A. Yes, I do, and we have.

Q. Has Johns-Manville notified every former worker of the implications?

A. Well, certainly to the extent that the policy exists, I understand. I obviously have not contacted the workers themselves, so I can't say how effective it is, any more than somebody buying a package of aspirin is going to use as directed.

But certainly the policy of informing people exposed to asbestos as to the confounding effects of smoking is something that should be done.

Q. Would you consider perhaps the corporate responsibility as well in notifying, provide an opportunity of help to workers to stop smoking as well?

A. I think that has been part of our program, yes.

Q. Is that part of your program for former employees as well?

A. No, it isn't.

Q. You would recommend this kind of a program to any of the corporations involved in asbestos, would you?

A. I would, yes. But I don't know how much weight that would carry.

Q. Are you aware of the fact that the smoking cessation program, or the smoking ban, at Johns-Manville in West Hill has been removed?

A. Yes, ma'am.

Q. I understand it's in response to a grievance from the union?

A. Correct.

Q. Do you not think that that's...how do you reconcile your policy with that?

A. I reconcile my policy with the reality of having the duly constituted representative of the union saying that while in fact this is a case, it is a work condition that they refuse to accept. Consequently, the imposition of this provides us with the necessary basis for filing a grievance against it.

Q. In the United States, however, you have pushed grievances through to arbitration on that, because of your real concern in this health matter?

A. We have gone to arbitration, yes, as I mentioned yesterday. At least three times that I'm aware of...I think perhaps one more, but I can't be sure.

Q. I think one of our concerns, and you raised it yesterday, is that concern about the fact that workers are presented with anti-smoking...or bans on smoking and smoking cessation programs versus compliance, and the actual smoking ban came in in June of 1975 in the Johns-Manville plant in West Hill, was my understanding. Is that correct?

I think you were here, actually, Dr. Kotin, around that time?

A. That's correct.

Q. Was that going to be a policy at West Hill?

A. Again, it was a policy of the corporation, and its implementation, obviously, was a phased-in implementation. I must say that I probably share the major responsibility for the ineptness, administratively, with which the program was implemented.

It was a little shocking to me...I had been in this industry all of eight or nine months at the time...it was a little shocking to me to realize that there was a special protocol, because I found a paradoxical situation of having the president of the local union tell me...and also the attorneys for the unions at grievances, emphasized again and again that the issue was not the biological basis for the ban, but items that...or aspects of the program that they felt violated collective bargaining agreements and employees' rights versus employer rights, and so on and so forth.

Other than to say that I was, I guess charitably, innocent - realistically, stupid, the program was just bungled, and I did the bungling because of my feelings that how could anybody really want to challenge this. It turns out that they really didn't want to challenge it, they wanted to challenge the packaging, as it were.

Q. I think, and that's what in terms of the Johns-Manville plant in West Hill, the smoking cessation program, or the smoking ban, rather, in the asbestos areas, came in at a time, would you say, of high publicity about the Johns-Manville plant?

A. That I can't answer. I really don't know.

Q. I think it was during a time when it was a debate in the legislature.

Now, I would like to go on to tab two, and that is your discussion of the Industrial Medical Officer and Corporate

Q. (cont'd.) Responsibility.

A. Yes, I have it.

Q. I'm sorry?

A. I have it, I say.

Q. Mr. Warren followed your distinguished career up to the time that you were a public health official, but what is that year and what date did you join Johns-Manville?

A. I joined Johns-Manville, I think it was June 1, 1974.

Q. Was anybody in that position, particularly, before?

A. They have had medical directors before, but Johns-Manville had its medical director leave some period before, and I think in discussions with the leadership of Johns-Manville, they felt that not only the additional medical skills, but perhaps they might be well advised to take a look at the total program in the area of health, safety and environment, which at that time was really not done on an omnibus basis anywhere, and to my knowledge is probably not being done anywhere in the country or perhaps...well, certainly in the country, that's all I can say... the way it is being done with Johns-Manville.

That is, to take the continuum of health, safety and environment, put it into a single program, have the leader of the program, the person responsible for it, at the level of a senior officer, and recognize that reporting to the chief executive officer and chairman of the board...and have this person develop a program which would, in an omnibus fashion, be concerned with...well, obviously first and foremost, the health of the workplace and the health of the worker, from which all issues are derivative, be responsible for the engineering, environmental engineering program, the industrial hygiene program, the EPA aspects of the program - air, water, solid waste, consumer product, have the education program in the area of health, safety

A. (cont'd.) and environment, have the...what I like to think is an academically oriented program in biostatistics and epidemiology, develop a library resource in the academic sense of the term of a library resource, and then have this program be the site for the corporation's activities in health, safety and environment.

I think it was unprecedented in two respects: First of all, the level of responsibility...I came in as a corporate vice-president with the understanding that if I were to stay on, after trying this new world of business, I would become a senior vice-president...which I did, I guess, in the traditional industrial sense. I am no more a senior vice-president than I am a pilot of a 747 in terms of my familiarity with the world of commerce. But certainly I am a senior vice-president in terms of the muscle that went with the position.

Over the seven year period that I've been with the company, now immediately before my retirement in a matter of weeks now, this program has evolved. I think it's been a model as measured by, if nothing else, the requests we have for the organization of our program, the visits of people in corporate engineering, corporate environmental control. corporate medicine, from around the country if not in fact from outside the United States as well, and gambling on somebody who, a corporation, who was an unknown factor as far as the world of commerce was concerned, and who in addition to throwing his M.D. on the table threw his ex-officership in the ACLU and the ADA, took one hell of a bit of courage on the part of Johns-Manville to do that.

They did it and I hope as they look back, they don't think they made a mistake. But that's for them to decide.

Q. You have described my next question, which was your responsibilities, but do most of your discussion here, you consider these your responsibilities? The medical officer as

Q. (cont'd.) a member of management, the responsibilities described on page 243 and on? I mean, I realize you are at a very senior position, but presumably these would apply to your position as well?

A. Yes. I wrote this with the...as one does write...with a combination of what the ideal is and hopefully where the ideal has not been met, there are efforts in the direction of achieving the ideal.

Q. Can I ask you if you are responsible in your program for your Canadian divisions as well?

A. Yes, ma'am.

Q. Can I ask you, exactly when do you think that you personally knew about health effects with asbestos, and what health effects?

A. Well, again I recall in the pathology textbooks of a noted Canadian, as a medical student back in the thirties, in Voigt's Second Edition of Pathology...and that's an old edition... there is a picture of an asbestos body and asbestosis.

Q. When do you think the general knowledge of cancer came about? When did you personally know about cancer related to asbestos?

A. I think in the 1955 publication of Doll and his associates on the Turner/Newell population really, as far as I was concerned, documented an increased risk to lung cancer, and then for mesothelioma clearly the landmark paper of Wagner, Slaight and their associates in 1960.

MR. WARREN: Mr. Chairman, I really wonder about the relevance of this line of questioning for purposes of this Commission. My reasons for concern are pretty obvious.

This could very easily become a backdoor vehicle for getting Dr. Kotin to discuss questions which are in products liability litigation in the United States, and the looseness of the procedure...and this is in no way to be critical

MR. WARREN: (cont'd) of the way we operate in this proceeding with scientific facts...but the looseness of the procedure employed here with respect to these questions of when did the scientific community know what about, when did they know what about what, particular kinds of disease, is something that I'm a little concerned about seeing addressed in this proceeding simply because the procedures are not such as they are in a court of law, and I don't want to get into a lot of formalistic objections. I just wonder if we can't cut off this kind of inquiry since I don't see that it has a lot of relevance to this Commission's undertaking anyway.

DR. DUPRE: Well, counsel, I take your point in that perhaps you are more familiar with the particular points that may be sub judice elsewhere, than I am. I must confess though that from what I've been hearing in the last couple of minutes, all I heard was a discussion that started out that was based on Dr. Kotin's article on the industrial medical officer, and at this stage, of course, I can't surmise that I know where Miss Jolley wants to go, but in response to two questions as to when he had found out something about any relationship of asbestos to disease, the answers that I heard are simply indicative that as his career progressed from pathology 101 at medical school, and when he read the Second Edition, on through to the mid-1950's, when he was obviously reading the literature, he seems to be right in step and very well read, I might say....

MISS JOLLEY: I would certainly agree.

DR. DUPRE: ...as a scientist.

But you may have good reason for having some worries about where the line of questioning is going, but Miss Jolley, where are we going here?

MISS JOLLEY: Q. All right. The next question moves on to exactly one of the areas of responsibilty - it's on

Q. (cont'd.) page 243...and that is on page 243, number five, and I think that's an excellent statement of corporate responsibility, and that is, "To use the standards established

> by regulatory agencies not as end points, but essentially as waystations to further reductions of hazards", and I certainly agree a hundred

percent with that statement.

The position that...is it true that corporations should know the guidelines or standards or whatever it is, in the jurisdictions that they are operating?

THE WITNESS: A. How do I handle this? I don't want to get myself...

MR. McNAMEE: Mr. Chairman, if I might have a word, I fully agree with Mr. Warren that sometimes the line of questioning can go too far. It is my understanding that the health effects of asbestos, and maybe Miss Jolley can ask for somebody from Johns-Manville to come in and testify as to corporate responsibility.

Maybe I shouldn't be saying this, but really that last question I think it totally inappropriate for this Commission, that he should be asked to speak for his masters on corporate responsibility.

MISS JOLLEY: I think that the head of occupational health, safety and environment should know what the standards are in the jurisdictions that the corporations are operating.

THE WITNESS: Miss Jolley, I have never met you before, but my understanding was, and the chairman said in his very kind introduction of me yesterday, that I was going to be invited back as a scientist...that indeed as a spokesman for Johns-Manville, my prior appearance before this Committee was clearly identified as such, and in rereading my testimony so as to make certain that everybody in the audience was aware, about

THE WITNESS: (contd.) every fifth paragraph, 'as an officer of the corporation', and I like to think that whatever knowledge I might have in the field of the biology of asbestos and asbestos-related diseases represents the basis for my...your very generous invitation for me to return.

DR. DUPRE: I feel that perhaps we are in a tricky area here, which is however, perhaps simply occasioned by the paper that relates to the industrial medical officer, that appeared in the book on asbestos-related disease.

Could I just call a recess for about five minutes, because I would like to confer with my colleagues on where we should go from here?

THE INQUIRY RECESSED

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THE INQUIRY RESUMED

DR. DUPRE: Dr. Kotin, my immediate concern is that you, yourself, should not be in any way in a state of confusion in terms of what our understanding about your visit is on the one hand, again on the other hand what the overall terms of reference and concerns of this Commission are.

You indeed have been invited here and agreed to come as a scientific expert to help educate us on the health effects of asbestos. That is a very, very important part of this Commission's terms of reference, and what you are contributing in that area we are very, very grateful for indeed.

That certainly in terms of your understanding of the purpose of this visit can be written 'mission accomplished'.

Now, what I want to simply put to you, Dr. Kotin, and indeed is a very useful reminder to all of us around here, is that our terms of reference as Commissioners, and our duties, of course, take us well beyond health effects. We do very much have to be concerned and look at development of health policies,

DR. DUPRE: (cont'd.) with the development of safety practices, with the implementation of such programs as seem advisable.

Indeed, it's not least because you wrote this most useful paper in the book on asbestos-related disease, about the industrial medical officer, that we eventually wanted to read that article ourselves for our own education.

Indeed, we ourselves have certainly a few questions that come to mind in this area. But let me put this to you, it is certainly our understanding that you came here on this trip to talk about the scientific side of things, and that you have been accomplishing very, very much to our benefit.

Now, I will simply put this question to you: Recognizing that we are going into something that is not directly related to the purpose of this visit, would you be willing, nonetheless, to help us, if you think you can, should we want to pursue a few questions from this industrial medical officer type of...or if, for that matter, one of the parties would like to do that?

MR. WARREN: Can I make a suggestion as to a distinction that seems to me to be appropriate, which maybe should satisfy all concerned?

To be sure, Dr. Kotin is here to testify as a scientific witness, and has testified, as we all know, about the scientific evidence for nearly a day and a half now.

In addition to that, this Commission's responsibility is to formulate public policy based on considerations including the scientific evidence, and obviously public policy implications can be derived from scientific evidence, and likewise Dr. Kotin has testified on that subject.

It is also true that Johns-Manville's corporate... Johns-Manville's policies, whether required by law or taken voluntarily, as the smoking program is an example, are likewise

MR. WARREN: (cont'd.) relevant to this Commission's consideration of what public policy ought to be formulated in the future.

The one particular area of questions which frankly I would object to, is the questions along the lines of who knew what when. It is those questions which pertain to the products liability litigation in the United States, where issues are raised about the past, in the fifties, sixties and forties, and I don't see that going back over past history and public policy in the past and so forth and so on, is germane to the scientific evidence number one, public policy implications drawn from the scientific evidence number two, or public policy taken by Johns-Manville now and in the future in response to scientific evidence, whether or not required as a matter of law.

I am trying to draw a distinction here which gives the maximum latitude to talk about the considerations which are plainly germane to the Commission's mission, and at the same time narrowly confine an area which deals with who knew what and when in the past, which I think as an attorney operating in this sense for J-M I think we ought to object to, and Dr. Kotin ought not to answer, simply because they are questions which are raised in a different form for a different purpose, and it's very difficult for me to see why they are germane here, nor can I feel totally at ease as to how answers to those questions might be misused in another form.

Do you see the distinction that I'm trying to pose?

DR. DUPRE: I see the distinction you are trying to make, and I realize that I could at this point get us into a long dialogue on the merits of exactly the points you have made, some of which, of course, are points in law.

Unless a counsel is going to consider what I am about to say is egregiously unfair, let me try to short circuit

DR. DUPRE: (cont'd.) it by simply making the following points: Without necessarily according Mr. Warren full value to the grounds on which you object, I am inclined to support no questions being asked at this juncture on who knew what when...among other things, for the very simple reason that the witness before us only entered the corporate sector in 1974, and that therefore anything prior to 1974 would be information that I certainly would imagine he could not possibly come by except on a second-, third-, fourthhand or anecdotal basis.

In putting forward my views, who knew what when is really not an appropriate or fruitful line to follow with this witness.

MR. McNAMEE: If I might add a word, the reason I registered my objection, I anticipate that...well, we're having a witness from the Ministry of Labour next week and I don't want him to be put in the position that he is going to be asked questions about Ministerial policy, why haven't you put in this standard, and what does the Ministry think about that, because we just really cannot...I can't say we can't allow it, but I think it would be terribly unfair to put witnesses from the government into that kind of position.

DR. DUPRE: Mr. McNamee, you, I think, are doing a very excellent job here of anticipating what may or may not come around the corner. Let me simply say that if and when those issues arise with the Ministry of Labour, I shall indeed be ready to entertain any objections to any lines of questioning on grounds which there are going to be rather different and with which I am, if I may say so, rather more conversant. These are grounds that have to do with ministerial responsibility, so on and so forth.

So what I have just said, counsel, does not necessarily hamper you in terms of whatever may be around the corner next week, two months from now, or whenever.

MR. McNAMEE: Thank you, Mr. Chairman.

MR. STARKMAN: Mr. Chairman, I would have to, at this time register our objection to this type of limitation being put upon the testimony of Dr. Kotin. As I understand it, Dr. Kotin was not called by the Commission, but was called by a party to the Commission with standing. He gave his evidence and we have full right of cross-examination on the evidence he gave, as well as cross-examination of him touching any matters which are relevant to this Commission's inquiry.

My friend says that some of these answers may have an effect upon litigation which is presently going on in the United States, and while I can sympathize with him, my only response would be that that is unfortunate and not our concern, and the Commission's inquiry should not be hampered by the fact that there are hundreds or thousands of lawsuits going on in the United States which touch upon similar matter. Otherwise, it would be impossible to go forward.

In terms of the cross-examination, there are two things. One, I think, is Dr. Kotin's credibility, and we are entitled to ask him questions as to his personal knowledge of what he knew and when he knew it, and what he said and when he said it, and what he meant by what he said. Those seem to me to be relevant questions in terms of their substantive value, and also as they go to his credibility.

But there is a further question which is, Dr. Kotin appears not only as a medical doctor and an expert in the field, but also as a senior vice-president of the Johns-Manville Corporation. I believe if you examine their corporate hierarchy, that's fairly close to the top in terms of where he sits and who he is accountable to. He was called as a medical doctor and as someone who is in that position.

True that he only began his employment there in 1974, but he may have knowledge of things that went on before 1974,

MR. STARKMAN: (cont'd.) and he certainly has access to the company records and documents.

To adopt my friend's submission, or to adopt the reasoning that you are not responsible for things which the corporation did prior to your apointment or employment, would be to absolve corporations of all responsibility because they are ongoing entities with constantly-changing personnel. And if you can say that anything prior to 1974 is not within the knowledge of Dr. Kotin, it would mean that we would never be able to get any information about what the corporation was doing.

Furthermore, it seems to me that one of the principle objectives of this inquiry is the question of standard setting, monitoring and enforcement. As I understand it, up until this time the monitoring to a large part has been in the hands of the various corporations, in the sense that they were carrying it out or it was done by their employees.

If it's going to be the Commission's recommendation that certain monitoring should continue and be done in certain ways, there is a question of who should do that monitoring, and that raises the question of the credibility of the corporation in how it carried out its monitoring in the past, whether it accurately reported its results, whether the monitoring was as full and fair as it might be, and whether we can in this jurisdiction continue to leave these responsibilities with the corporation or whether it has to be taken over by other persons or agencies.

Furthermore, the question of the credibility of the asbestos industry...or in this case in particular of Johns-Manville...and the way it has carried out its operations, raises many questions about how stringently the company...this company... must be supervised by other agencies, be it government or otherwise, in its day-to-day workings.

So I think for those reasons the questions of what

MR. STARKMAN: (cont'd.) the corporation knew and when it knew it, and what it has been doing over the past...over the foreseeable past...are very, very relevant.

For my friend to object to these questions after calling a witness who is also a senior officer of the corporation seems to me to be unreasonable and denying us our rights of cross-examination at this inquiry.

MR. WARREN: Mr. Chairman, I would make only one very brief response to this. Were this a court of law, which it is not, virtually every question that has been asked by Miss Jolley would be an inappropriate question because it would be a question which goes beyond the scope of the direct testimony presented by Dr. Kotin yesterday.

I haven't objected to that...this isn't a court of law.

MISS JOLLEY: This is not a court of law.

MR. WARREN: I don't intend it to be, I'm not suggesting that it should be. This is a Commission of Inquiry, and as I stated earlier, I have absolutely no objection to questions which go beyond the scope of the direct testimony, which go to questions of public policy, which are relevant in a broad sense, probably, to this Commission's function and objective and aim.

I believe logically, honestly, every other way, these questions which go to culpability...if that's the word I can use...don't really have much, if anything, to do with what we are talking about here today.

I would suggest though, just as is almost always the case with procedural objections, the better thing to do at this juncture, rather than sit and debate ad infinitum abstract questions, is to proceed with the questioning and if I have problems along the lines that I have laid out, and tried to lay out as clearly as I know how, I'll interpose another objection

MR. WARREN: (cont'd.) and I'll try to be clear and concise when I do so. But I think it makes more sense right now, having heard the sentiments of all, to proceed and let's see where we go rather than continuing to debate this point.

THE WITNESS: Mr. Chairman...may I make a comment, Mr. Chairman?

DR. DUPRE: Yes, I wish you would, Dr. Kotin.

THE WITNESS: My guess is, it's almost going to be, I hope, not Solomonic, but I will rely on my training for the rabbinate as the basis for it.

I'm sure Miss Jolley, whom I've never met before, has done a fair job of learning who I am, what I am, and it should be clear even from the day and a half I've been here, and from my testimony here and before the other agencies that are contained in this book, that it's alien to me to duck questions, and if this hadn't been...it obviously pointed up a dimension that I am unaware of.

I would like to make a suggestion. I think I have seen Mr. Warren three times in my life. I think this is the third time I have seen him. I'm sufficiently innocent, as I was in trying to deal with introducing the smoking program, to have not even thought of the things he raises. But the minute he mentions them, they become very, very pertinent.

I would be delighted to come back...in my wildest dreams I can't conceive of a question that Miss Jolley or any of her associates can ask that I haven't been asked before and that I'm not prepared to answer, short of my ethics and my morals, and how I treat my wife.

I would like to come back, but with a Johns-Manville attorney at my side. I do this with really no great feeling of sacrifice, because it's great to come back to Toronto, it's a great place.

I would feel much more comfortable about that, and it's obviously not a matter of...it's not a ploy to buy time. The

THE WITNESS: (cont'd.) record is here and clearly having written what I've published, I believe, and if I have changed my point of view, I have probably published that.

I recognize the Commission has time constraints as well. I will do everything in my power to arrange a mutually satisfactory time to...as the Supreme Court says, with all deliberate speed. If that's acceptable to you, I would be very, very happy, and it would keep me out of trouble in terms of, as counsel there said, the not hundreds but thousands of cases which cover the spectrum of third party tort, I'm told.

I don't know what I can or cannot say from a legal point of view, just as I'm positive of what I can say from the point of view of the substance of any response that I have, and it's comforting to know that when Mr. Meany and Mr. Kirkland appeared before Commissions that they had their retinue of attorneys just as the chairman of the board of DuPont and Dow have their retinue of attorneys when they appear before commissions as well.

I would like that privilege, and this being summer, I would be glad to come really at a time that would be sufficiently soon that the continuity would not have been lost, or the momentum would not have been lost.

I think that's about as far as I dare go in light of what Mr. Warren has brought up. I will be delighted to come, and I will come as senior vice-president of Johns-Manville, and that should immediately remove many of the caveats that have been uttered today.

MR. WARREN: I would suggest that Dr. Kotin has put his finger on one obvious aspect of this, and that is while I have awareness of in general...and I mean very general knowledge of...the products liability litigation that is pending in the United States, I am no expert in it either, and don't...am really not in a position to see around every corner and know

MR. WARREN: (cont'd.) every potential implication with respect to that litigation.

I would, again, kind of come back to my suggestion at the end of my last remarks, and that is maybe we ought to see how far we can go and we may find out that Miss Jolley is a lot more able to carry out her lines of questioning, include everything she wants, and maybe Dr. Kotin won't have to come back, but if it got into very, very rough going, I think that what Dr. Kotin says is a really very sensible suggestion.

THE WITNESS: I would...may I, Mr. Chairman, make a comment? I notice that there are issues of a memo on Johns-Manville letterhead that has my signature, there is a copy of a Johns-Manville inhouse publicaton today, and I'm sure there are other documents which I am delighted to be questioned about. I have no qualms about responding and I would just like that added bit of comfort, because as of now I'm uncomfortable and let me even say it...I don't think I'm a coward...but I'm fearful, and I would like to have the benefit of counsel because of the fact that there are implications that I am unaware of.

I know about enzymes and cancer. I really know nothing about...so if this would be agreeable, it is no great burden to return to Toronto, but actually it is, you know, there is a series of time commitments that have been made. I would be even glad to do a little calendar shifting and what have you, to come at the earliest possible moment consistent with the needs of the Commission, because I think I understand and have great sympathy for the position that you take, sir, that there is no way you can put my right hemisphere devoted exlusively to science and my left hemisphere devoted to my administrative position in the corporation. It's a strange thing.

I just don't want to be put in the 'dusty way to death' situation where things have been taken and quoted out of context, as I say, to the point where even Mr. Goldenson, chairman

THE WITNESS: (cont'd.) of the board of ABC, had the kindness to call me up and apologize for what he thought was some yellow video journalism.

MISS JOLLEY: I would like to say, Mr. Chairman, that the intention of the questioning was to deal...because I think all of this does in fact deal with health effects, and we have a legacy of past practices here, as well as you have in the United States. We don't have product liability litigation to provide us...and that's not our interest here, and culpability is not. It's responsibility we are interested in, and I think that more importantly there are Johns-Manville workers right now, all around in Ontario, that have been in your employ since 1974, and there are a lot of questions to ask about exactly that, and it has everything to do, I think, with health effects and everything to do with your testimony yesterday, and the results of the exposure. So I don't think my line of questioning was out of line.

THE WITNESS: I ain't ducking you. I just would like to be a little more secure, no less than...

MR. WARREN: I would once again suggest that we try to proceed and see if...

THE WITNESS: All right, let's go.

MR. WARREN: ...see how far we go. I mean, we may find that Dr. Kotin is uncomfortable, or I may be vicariously objecting on behalf of some counsel out there who know a lot more about this issue than I do, but I suspect it makes more sense...

MISS JOLLEY: I wonder, Mr. Chairman, if we could have a recess for a short...

DR. DUPRE: You would like a recess? Thank you. We'll recess for about five, ten minutes.

THE INQUIRY RECESSED

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THE INQUIRY RESUMED

DR. DUPRE: We are now reconvened, and we had this last recess at the request of one of the parties. Does any party wish to say anything at this point?

MR. McCOMBIE: Well, off the record...Dr. Kotin indicated off the record something. I am wondering if he is willing to indicate that now on the record?

THE WITNESS: Yes. What I would like to say is that in view of the constraints associated with the legal status of the corporation, I feel that I would like very much to have the benefit, no less than Miss Jolley has the benefit, of having an attorney available for consultation.

MISS JOLLEY: I object to that. I don't have an attorney.

THE WITNESS: And I would be glad to return if the Commission is kind enough to invite me to return, with counsel, with the full understand that the rules of the Commission make it proper for anybody in the audience to ask me questions.

MR. McCOMBIE: Can I just ask one question, and that is whether or not Dr. Kotin is aware of the fact that this will be accepted by his legal counsel in Denver. One of our concerns is that he be advised against returning.

THE WITNESS: I can guarantee you that I will return. I won't walk on water, I shall return.

But seriously, I'll be back and I don't know how to state it more emphatically.

MR. McCOMBIE: So you will undertake personally to be back, as a personal undertaking?

THE WITNESS: I'll be back. The mechanism for my return, I think, is probably a second order issue. I'll be back.

MISS JOLLEY: Could I ask, Dr. Kotin, if at that time that we would like to deal with all of the material that was submitted, and that would be the corporate responsibility

MISS JOLLEY: (contd.) and industrial medical officer, and also your testimony before the Senate on the compensation bill, and that kind of testimony.

THE WITNESS: I will ask any and every question that I am not proscribed from answering by my attorney, and I really don't...I can't postulate or suggest what the attorney will or will not let me answer. But by the same token, Mr. Chairman, I'll be hung for this, but obviously after September 1st, I'm a private citizen.

I guess I'm one now, too, but I will be coming... and all I want is the benefit...I want to do no harm, in the best medical tradition of primum non nocere, I don't want to harm...not only do I not want to harm people, I don't want to harm the corporation as well by just inadvertence or by impropriety.

I think that's fair and I would be glad to give you the phone number of the people we were speaking about, anybody...Peg Seminary or George Taylor, Shelley...and find out whether I will show up if I say I'm going to show up. These are officers or employees of the American Federation of Labour at the Congress of Industrial Organization.

DR. DUPRE: Dr. Kotin, just in terms of the point you last raised, your offer to come with a J-M counsel to protect that side of the situation, is one that holds good after August 31st.

THE WITNESS: That's correct.

DR. DUPRE: As well as before.

I wanted to get that point on the record, because from the standpoint of the Commission, your appearance then, should we accept your very kind offer, will be of far greater value to the Commission after August 31st...indeed, quite possibly some few months after August 31st, than it would be beforehand.

DR. DUPRE: (cont'd.) The parties here are aware, as naturally you would not be, that we will have formal testimony on matters that include standards and enforcement, and for that matter, some compensation problems. What we have...how we have phrased this is to take place at the time that the results of the research that our own staff is conducting will have been available to the Commission and to the parties as well.

So I take it that I can look at your offer to return as one that has a time span that could well be into the fall or early winter?

THE WITNESS: It's open-ended, sir.

DR. DUPRE: I appreciate that.

THE WITNESS: Thank you.

MR. WARREN: I would just add that I think it is in that phase of the hearing that the questions which we have been disputing about are most relevant, if they are relevant. I would subscribe very much to that sense of ordering about these proceedings, because as you saw yesterday from my own direct examination of Dr. Kotin, that direct examination was aimed at biology and things very esoteric, I'm afraid, but pretty doggone far afield of the kinds of issues which are in dispute.

THE WITNESS: If I may make one additional comment, and I promise not to say another word, included in my bibliography...or not included in my bibliography...are several, I won't say how many, documents, publications, reports that were prepared incidental to my responsibility in the area of standard setting, scientific base for regulation, and so on, that were submitted in response to a congressional mandate...my annual testimony before Congress defending my budget each year. They wouldn't be included in a bibliography, but as long as there is a four to six week period that exists...they address really the issues of what constitutes the scientific basis for regulation, what are the elements in policy making and so on.

THE WITNESS: (contd.) I would be glad to submit them. The reason they weren't included here is because they were completely alien for the purpose that I thought I was coming for. But in the area of the fall and early winter discussions, I would be glad to submit them for what they are worth. They are just so much prose, but nevertheless I did have this responsibility for ten years and I would be glad to submit it.

DR. DUPRE: Now, just one point at the moment to settle the possibility of Dr. Kotin's return, the Commission takes this offer as tabled. The Commission, of course, will reserve to itself the decision as to when and under what circumstances, and at what time, Dr. Kotin would be invited to return...but as usual, will be guided by the discussions with the parties in terms of the appropriateness of the timing, and so on.

I should now make, perhaps, one other point, because of something that arose on the record to which Miss Jolley objected, and of course this was completely inadvertent, on your part, Dr. Kotin, since you have thankfully been excused from any of the procedural developments of this Commission, but I will simply point this out for the record: Miss Jolley is in no sense here with counsel. Miss Jolley, indeed, is, in her own right, the agent of one of the parties with standing, the Ontario Federation of Labour, and of course is in relation to that particular party, as for example Mr. Warren is to the AIA, or Mr. McNamee to the Government of Ontario, and so on.

The fact that Miss Jolley is not a lawyer simply reflects the very firm view that I have had of this Commission from the beginning, that among other things, of course, it is not a make-work project for the legal profession, which indeed accounts for why we have counsel, legal counsel, who are not licensed to practice law in Ontario, whose expertise endowed in

DR. DUPRE: (cont'd.) M. Casgrain and Mr. Warren and their colleagues, we so very much appreciate.

Of course, to touch all the procedural bases, because I consider them most important, one of the fundamental reasons why we are not a make-work project for the legal profession, I would remind all of you, is that the purpose of this Commission, its prime and central focus, is not...as I said at our very first meeting...to investigate allegations of past wrongdoing. Our prime focus is instead to formulate recommendations on legal policy, administrative and other changes, for the consideration of the government.

Insofar as things have happened in the past, either right or wrong, there can certainly be some relevance to recommendations in the future. But past practice is a secondary and to the extent that we go into it, a supporting feature of the prime focus which I remind all concerned we must never forget - that the prime focus of this Commission is to look at recommendations dealing with the future, and not to deal with allegations or otherwise of wrongdoing that involve individuals.

This was plain, of course, from the day the Commission was first created, and for that matter appointed, because among other things, Dr. Kotin, even casual observation, I'm sure, will have made it plain to you and to everyone else here that I am not a judge.

All right?

Now...

THE WITNESS: May I apologize to Miss Jolley. I'm awfully sorry. I would like that to be on the record.

M. CASGRAIN: It's no insult to say that someone has a lawyer with them. You don't have to apologize.

MR. WARREN: You could look at it another way. Dr. Kotin was trying not to accuse her of being a lawyer.

DR. DUPRE: In this jocular mood, even though

DR. DUPRE: (cont'd.) it's going to show up on the record, I simply want to point out to Mr. Warren that one of the reasons why I'm very conscious of the standing of all of the representatives and the parties in front of us is that...you'll never believe this...but the last incarnation in which I had the misfortune of having to be involved in an inquiry, Mr. Warren, had to do inter alia with the regulation of the legal profession in this province, and I know that with due respect to you and M. Casgrain, there are any of a number of individuals who naturally out there would not consider either of you gentlemen as counsel for one moment...most especially because you are not licensed to practice in this province, and thereby are seen to interfere with livelihoods.

Very well, Miss Jolley, you still may continue to ask Dr. Kotin questions, and perhaps Dr. Kotin, given your offer, anytime she has a question that you feel you want to defer to later on, simply say so. But I am assuming that Miss Jolley still had some questions to put to you.

THE WITNESS: May I respectfully suggest that I'm apprehensive, I'm not relaxed. And again, I would very much appreciate the opportunity of a return and return in a way that would make the questions that would be, I think, incidental to the material that she has on her desk...they would be fair game questions and I would be doing a disservice to the Commission, and to Miss Jolley, and to the things I believe, if I ducked them. So I will be as candid as I can.

DR. DUPRE: I would assume that Miss Jolley might still have some unanswered biology 101 questions. That was all, Dr. Kotin.

THE WITNESS: Okay, thank you.

DR. DUPRE: If not, we'll simply ask...

THE WITNESS: Go ahead. If you have...please, go ahead. I don't mean to arbitrarily...

MISS JOLLEY: This is on the understanding, of course, that the broader questions can be answered in the future.

MISS JOLLEY: Q. I'm sorry, Dr. Kotin, there was one thing that you did have in your testimony before the Senate Committee, and I can't refer you to the date, but you said something...or the actual page number...but it was interesting because we have had a lot of testimony before this Commission on the very bad outcome of people with asbestosis, or the potentially bad outcome of people with asbestosis, and there was something in your testimony...and I apologize, I was not following that train of thought as you...but you indicated that there was some reason for optimism of treatment of asbestosis, and I wondered if you could...

MR. LASKIN: It's 523.

MISS JOLLEY: Page 523.

DR. DUPRE: Miss Jolley and Dr. Kotin, if you will permit, I had something here that I was saving for what we call the Children's Hour, which is when the Commissioners finally have a chance to pose some questions, but because I do, I can simply point out to you that it's page 523, at the bottom, where I believe you expressed some optimism with respect to the treatment of asbestotics.

THE WITNESS: A. Right. Indeed I do, and since I am not a clinician, I am using the data of Dr. Hans Weill, Dr. Edward Gensler...Dr. Hans Weill of Tulane University, Dr. Gensler of Boston University...but mostly the work of Dr. Selikoff at Mount Sinai Hospital, where Dr. Selikoff on record before lesislative hearings has emphasized that we have moved from the era where asbestosis need be regarded as a life-shortening experience, and I think this makes some sense, particularly in view of the fact that the deaths from asbestosis in the past were to some degree associated with the secondary effect of fibrosis of the lung on the heart, producing what is technically known as a lung-effected heart corpulmonale, and

THE WITNESS: (cont'd.) with enlargement of the heart ultimately leading to heart failure.

But by and large, the prognosis, the grave prognosis on asbestosis in the past was due to the hypersusceptibility of the lung to secondary infection, to the formation of pulmonary lung abcesses, to pnemonias...or pneumonitis would be a better term, inflamation...an infectious inflamation of the substance of the lung, and also the confounding effect of cigarette smoking in persons who were asbestotic. So that with proper care, the judicious use of antibiotics, the judicious application of pulmonary therapy... there is, only within the past decade at the most has there been the discipline of pulmonary therapy at the technical level, where people are taught to maximize the use of what remaining functional tissue they may have...the cessation of smoking. All of these have added up to, as I...and I again would be delighted to bring it with me...the actual data and quotes, abstracts from the testimony of Dr. Selikoff, both the scientific meetings...I believe actually in the current issue or the new edition of Preventive Medicine, the standard textbook of preventive medicine, Rossenhauer, there is a chapter there that Dr. Selikoff has written. There are frequent references to this.

There seems to be that unanimity, no matter how much disagreement there may be between doctors...it's interesting I chose these three...between Drs. Gensler, Weill and Selikoff on a variety of substances, of aspects of the problem, on this there is consistency, that asbestosis is, as put there, you can beneficially impact on the prognosis of the disease.

This isn't to say that you can reverse fibrosis, because in fact you cannot, of course. What you can do is maximize the effectiveness of the remaining functional lung tissue you have.

MISS JOLLEY: Q. What is your sense of the impact on the prognosis of lung cancer and mesothelioma at this time?

THE WITNESS: A. Well, obviously I believe, as I said earlier, that compliance with regulations in the United States should have a protective effect.

Q. I'm sorry. I meant medical intervention on behalf of patients with lung cancer and mesothelioma.

A. The treatment of mesothelioma, morbidity and mortality can be treated as unity. For lung cancer, well, the prognosis of cancer in general is more a reflection of the evangelism of the physician you are speaking to, frequently, than sound scientific data.

I don't know of any substantive improvement over the last several decades in the prognosis of lung cancer, at any given stage in the disease. Clearly, those who have diagnoses made very, very early have a better...have a potentially better prognosis because of the natural history of the disease.

If by sputum cytology a noninvasive cancer is discovered, clearly this is a disease that I think probably can be referred to as curable. This is a very small percentage, but that was always the case.

Our knowledge of the biology of cancer as a factor in improving the prognosis of cancer over the last several decades has been sort of a tragic disappointment, at least to me.

MISS JOLLEY: Thank you, Dr. Kotin. I look forward to you coming back and cross-examining you.

THE WITNESS: I look forward to returning, and I don't say that with any wry or unspoken addenda. I do look forward to coming back.

Thank you, Mr. Chairman.

MR. LASKIN: I don't think we are quite finished.

MR. WARREN: I think we've got some more biology maybe here from somebody.

MR. McCOMBIE: Just to introduce myself to Dr. Kotin, my name is Nick McCombie, and I'm here representing Injured Workers Consultants.

Like Dr. Kotin, I'm now feeling somewhat nervous about the questions that I wanted to ask directly related to biology, but hopefully I'll keep within that framework.

CROSS-EXAMINATION BY MR. McCOMBIE

Q. I wanted to go over a couple of things that were mentioned yesterday, and the first one, which is something that Miss Jolley referred to earlier today, was the idea that a healthy, nonsmoking asbestos worker could expect to have anywhere between ninety-five and ninety-nine percent effectiveness in the defence mechanisms of the body. You indicated yesterday that that was true up until a certain point of exposure, where obviously those defence mechanisms would break down.

I'm wondering if you can give us any kind of idea of that level?

A. There are no quantitative data for that, other than basically one of the principles...I'll use formulating as a principle for the moment...of occupational medicine is that if you are going to find something...this has nothing to do with asbestos necessarily...you are going to find an occupational disease, the place to look first is in maintenance men, because they are the ones that are going into trouble situations, necessarily, and they are getting peaks.

So there are...that's the extent of the quantitation. We know they get that excessive peak exposure, they are going in to unplug a line or put a new gasket on a valve or something like that, so there is no numerical one, but it accords with all the things we know about the pathogenesis of disease, both occupationally and nonoccupationally. There is no number.

Q. I'm wondering if you can tell us then the line above which the exposure would override the defence mechanism. If it cannot be defined, at least can one say that it's an exponential decline in defence mechanism, or is it one that slowly deteriorates?

A. No, it isn't exponential. It's, I think an attempt to address this is the incorporation, at least in the United States, in the regulations, a peak exposure limit as well as a time-weighted average exposure limit.

Now, let us arbitrarily say that that peak exposure limit in the minds of some...and it would vary for everything...expresses concern over just what we are talking about, an exposure that might overwhelm a defence system.

Q. Okay. I would like to move on to a couple of other things that...or one thing in particular that Dr. Mustard was asking about yesterday, and it concerns the animal experiments that were done with asbestos. I believe Dr. Mustard was asking you whether or not there were indications that there was fibrosis prior to the development of cancer in rats, I believe it was.

A. Yes, sir.

Q. Your answer then was that...?

A. I believe there was. In fact, the more I think about it, the more I am convinced. I can see the photomicrographs in the paper by Dr. Wagner in the British Journal of Cancer.

Do you have a copy of his paper there? Oh, no, that is in the Lyon Conference.

But this is a paper published in 1976, or something like that, and one before.

But again, that is easily verifiable.

Q. Well, as Dr. Mustard pointed out, and I hope I'm not being naive, but the rats were not smokers and I'm wondering how you would account for the fact that these animal

Q. (cont'd.) models developed cancer without the codeterminant of the smoking that you...

A. Oh, I think my testimony has repeatedly said I recognize the induction of cancer in nonasbestos cigarette...in the nonsmoking asbestos workers, and specifically pointed to a bibliographic reference now some six or seven years old where I identified in a table bronchiolar cancer as being a cancer associated with excessive asbestos exposure with absolutely no reference to cigarette smoking in that. It's just that the overwhelming dose given to animals in experiments models, by design...and as I said yesterday, the rationale for the high exposure is the belief that one can telescope in time the evolution of a desired end point by increasing the dose.

This is why animals are usually exposed to the maximum tolerated dose of an agent. Now, I don't remember exactly what the exposures were in Dr. Wagner's study, but they were high. And understandably so. He was looking for an end point.

Q. Thank you. There was one other question which more than anything I think I would just like some clarification on, and hopefully I'm not treading on too thin ground here.

Again, it's referring to the paper that caused all the ruckus before, but hopefully it's a little bit less contentious, which is tab two, on page 240. The second paragraph down there, if I could just quote from that, you say in here, quote: "The population is also changing, not only in numbers,

> but also in its characteristics. Many, many people are now alive as a result of the therapy they have received. This therapy which is salvaging people with diseases that were fatal thirty or forty years ago, is obtained at a cost - depletion of physiological reserve. This has, in turn, created a growing segment of the population

Q. (cont'd.) "with lowered susceptibility to the adverse effects of environmental agents." End quote. I'm just wondering if you could possibly expand on that just a little bit, as to exactly what you are meaning here?

A. What I'm meaning is, I think, very briefly stated...first of all, I think it says it in what is for me a rather uniquely concise way...that there is no question that persons with chronic disease, chronic respiratory disease, chronic diseases of the liver and biliary system, of the kidney and urinary system, but most noticeably persons with disease of the cardiovascular system are now being kept alive. Persons with decompensation of the heart that have as a corollary some impaired circulation to the totality of their organ systems because of a failing heart now are being kept alive for a much longer period of time, and the price that they are paying is a decreased reserve, a decreased, less-than-optimal physiologic state, and these represent a segment of the population.

This is manifested by, disease aside, just there is a fibrogenetically built-in senescence, and I'm speaking of senescence in the noncultural sense. I'm speaking of senescence in the tissue/organ sense. There is a built-in senescence in all of our tissues. We lose elastic tissue as the decades go on, which is a manifestation of senescence. We have interference with circulation so that part of the functional part of organs is replaced by connective tissue - scarring of the heart muscle, scarring of the kidneys, are all reflections of passage of time, and they vary.

This senescence, physiologic senescence, in the past was...made people with this decreased reserve as a special prey for exogenous agents. Now we are handling these people medically in the sense of keeping them functional.

Q. So if I understand you correctly, the threshold level that we would have looked at in a lot of agents forty or

Q. (cont'd.) fifty years ago, if we can, with the benefit of hindsight, go back and say fifty years ago the threshold level of agent X should have been whatever, that there has been a change in the general population to the extent that that threshold level, with the increased susceptibility that you are talking about, should be lowered?

A. Not necessarily, because it depends what your end point is. If it would be for certain toxins which depend upon liver metabolism for detoxification, and a person has fibrosis of the liver, that might be one thing. For cancer there doesn't seem to be...the induction of cancer is minimally, if at all, affected by the age of the animal system - including humans - that is exposed to the carcinogen.

So there is no answer that would cover the entire substance. You would have to deal with it on an individual basis.

Q. I would just like...I have some other questions but I think that they are probably best to be deferred to your return. But one final question that I am interested in is the question of threshold, and I think that I'm correct in saying that you believe there is a threshold level, it's in a lot of the literature that we were given that you have written. You indicated there was a threshold level for virtually all carcinogens, is that correct?

A. I think there is a threshold level for the induction of cancer, very much so. Yes, sir.

Q. Is there a threshold level for cigarette smoking?

A. There surely is.

Q. Do you have any idea what that threshold level is?

A. I think Dr. Hammond's data suggests that five cigarettes a day or less. I don't know...this was the original data...I'm not sure that he hasn't revised it one way or another.

Q. I see. So five cigarettes...

A. Again, these are not my data and, happily, they are the kind of data that I don't remember, because you can easily get them by looking at the most recent Surgeon General's report. You are aware that the Surgeon General has to issue an annual report to Congress on the status of smoking and health, and these data are there very precisely and the annual trend is discernible by looking at every annual issue from 1964.

Q. But the no-smoking program which you were discussing yesterday is designed to have Johns-Manville employees quit smoking altogether, rather than go to the threshold level of cigarettes?

A. Oh, no. You see, basically Johns-Manville, for all its imputed omissions, really has the worker eight hours a day, and it really has no way of...and wouldn't...tell a worker it couldn't smoke the sixteen hours that the worker is not in the Johns-Manville employ, on a daily basis.

The name of the game, and we are fully aware of this of course, the name of the game is to reduce smoking, one, at a time when opportunity for simultaneous inhalation of asbestos exists. Number two, historically those who have been able to kick the habit are those who have been, by whatever technique possible, been subjected to progressively reduced dose of whatever it is that is habituating in cigarette smoke - probably the alkaloids. In fact there are many commercial products on the market which base their effectiveness in getting you to conquer the smoking habit on the fact that you have filters that you change and they reduce the amount...and low-tar cigarettes clearly are the ones which yield the greatest number of excigarette smokers, if you were to categorize the source of excigarette smokers. You will find they come predominantly from people who have shifted from the traditional Camels, high in...I hope Reynolds doesn't sue me...to, let me one of their own, Vantage I think is their very low-tar cigarette. So there is every reason

A. (cont'd.) to assume that despite our eight hour, or the ten hour, that the person...whatever it is...on a given day that a worker may work, is the period he is not smoking, it is clearly moving him in the direction, along with the other activities that are available, to become an exsmoker.

Q. So the ideal is to have the person the, I believe you mention their spouse, give up smoking altogether?

A. Yes, sir.

MR. McCOMBIE: Okay. I have no further questions.

DR. DUPRE: There will be questions from other parties, and from the Commissioners, but Dr. Kotin, I am now hyperconscious of the fact that we have exploited you for fully four hours and a half, since eight o'clock. Perhaps at this point I should offer to break for lunch until, say, two?

MR. LASKIN: That's really in the hands of the three of you, because there are no other counsel who have any questions left.

DR. DUPRE: M. Casgrain, you have no questions?

MR. LASKIN: Mr. Starkman is going to defer his questions, so it's really up to the three of you and Dr. Kotin.

DR. DUPRE: Well, Dr. Kotin, we are in your hands. We might have anywhere from half an hour or a little more...

THE WITNESS: Why don't we do it now then?

DR. DUPRE: You would rather do it now?

THE WITNESS: Yes.

DR. DUPRE: Okay.

All right, Dr. Uffen?

DR. UFFEN: I am intensely interested in the basic biology you were discussing yesterday, in particular what we were referring to, I think, as solid carcinogens.

In the back of my mind all the time was the problem we have to face some day about substitutes. In order to focus what I would like to extract from your experience, I could refer to

DR. UFFEN: (cont'd.) page 523 of tab six. This was when you were testifying at a previous hearing.

It deals with manmade mineral fibers, and there is...the second paragraph from the top of the page:

> "Clearly, those who have studied the problem are aware that the body handles manmade and mineral fibers in a different way. It fractures the fibers differently - that's physical. The rate at which the fibers can be dissolved by tissue is different - that's chemical".

Could you explore for us the implications to, say, a borosilicate glass as compared to an asbestos fiber? Would there be any biological theory that would help us understand the difference?

THE WITNESS: First I think one would say that the principle of carcinogenesis that applies to an asbestos fiber would apply to any fibers - a titanium fiber, an aluminum whisker, a carbon fiber, an iron filing, or a manmade vitreous fiber, and it can be an aluminum silicate glass like a ceramic fiber, or a borosilicate glass as you say.

So all other things being equal, a long, thin, manmade vitreous fiber in experimental model systems, particularly - virtually exclusively, because inhalation studies on glass are just being completed, but by the intracavitary installation behaves for all the world the same.

Dr. Stanton, Dr. Pott, Dr. Wagner and Dr. Davis have all produced tumors by intracavitary installation.

DR. UFFEN: In animals?

THE WITNESS: In animals.

So the question then one asks is, what is...are there any possible differences that would mitigate against the glass fiber producing an analogous disease to asbestos. The effectiveness of any fiber in producing disease is dependent upon

THE WITNESS: (cont'd.) what we call the 3-D phenomenon - dose, durability and the disposition in the tracheobronchial system, or anywhere in the body.

I have some data here that might be useful. When one looks at dose, durability and, of course, dimension, one...well, let's eliminate dimension immediately by saying what applies to an asbestos fiber in experimental models has applied to a vitreous fiber glass. In terms of dose, again the Stanton stuff has clearly shown that dose is a reasonably constant thing in terms of, again, intracavitary installation.

So what you are left with is the discriminating... any discrimination between an asbestos fiber and a glass fiber is durability, and here you have substantive differences between asbestos and manmade vitreous fibers.

I guess just from the point of view of basic understanding, it is well to remember that asbestos is a crystalline material, and your borosilicate glass is an amorphous material.

DR. UFFEN: The glass is devitrified.

THE WITNESS: Oh, yes. I'm sorry. Devitrification of glass will result in it, but you don't have the silica oxygen/hydrogen bonding in glass, the covalent binding, that you have in an asbestos fiber of the magnesium...all right, so what you have, if I may go to the board, sir, is several things that happen, and this can be demonstrated, it is demonstrable experimentally and it has, I think, compatible clinical counterparts.

Just as we agreed that the effect of a chrysotile fiber, for instance, fracturing or splitting into fibrils moves it in the direction of increased pathogenicity, a glass fiber, because it is amorphous and does not have this covalent binding, when injected or placed in animals, fractures horizontally. So that actually you are moving towards shorter fibers which moves

THE WITNESS: (cont'd.) them away from what we like to consider as the criteria for pathogenicity.

Secondly, when you use an array of accepted models for tissue fluid systems - accepted because they are the nutrient media for cell cultures or nutrient media for organ cultures or synthetic plasmas or serums, you find that this amorphousness is also reflected in a more rapid rate of cell utilization.

Now, this rate varies from vitreous fiber to vitreous fiber, so that for ceramic fibers, probably, aluminum silicate fiber, it appears that it probably has a slower rate of dissolution.

But these are data that are being accumulated. So that is the second factor of durability which tends to suggest that manmade vitreous fibers may not be as hazardous as asbestos.

Then when one looks at populations exposed to manmade vitreous fibers, who have been exposed for a long enough period - and not to say nothing can't happen in the future - but you have three very large populations, a population of about six thousand workers in 1943 has been followed until 1981, literally, and this is a group of workers who were exposed to manmade vitreous fibers of a very thin dimension making flotation fiber for the navy in World War II. This is when fiber glass was being substituted for kapok and other materials.

So you have that population. In addition, you have a population that is...the number isn't really very hard, but circa a hundred thousand...persons exposed to mineral wool production, and mineral wool has been produced since the turn of the century.

The interesting thing about all fibers that are produced, manmade fibers is, that though you target production for a nominal diameter, you obviously never really succeed. So what you have, if you want a nominal diameter for insulation fibers of let's say five micrometers in diameter, you are going to have some that are going to be more than five, and some that are

THE WITNESS: (contd.) less than five, and some that are less than three, and some that are less than two.

So you have a population that has been exposed for something like seven to eight decades to a mineral wool which has had a variable component of fibers which fall into what we consider the pathogenic range.

Then you have a third population of those really exposed to insulation glass itself. Now, insulation glass is thick fiber. Compared to the pathogenic dimensions, insulation glass would be like hawser rope, really.

And there you have again, depending upon the figures, perhaps thirty-five thousand workers.

Now, what is unique about these workers is that first of all the very nature of the manufacture of vitreous fibers, and the nature of the vitreous fiber itself...and this has all been published in the literature...tends to make the glass less likely to be airborne, less dusty than asbestos.

But if we accept the fact, as I think everybody does, that no evidence thus far of any fibrosis or lung cancer or mesothelioma has been identified in workers in vitreous fiber. One such report from Japan was made two years ago and I got a free trip to Japan out of it, but basically this was a report by Dr. Saammo and his associates, which since has been repudiated by Dr. Saammo.

But the one thing that one keeps looking for if it's going to have an asbestos-like reaction is the presence of pleural changes, because while there may be differences in opinion as to the prognostic significance of pleural changes, the pathogenesis of pleural changes, there is nobody that questions the fact that pleural changes are stigmata of exposure to asbestos.

Now, it's inconceivable...and I use the term in its strictest connotation...that glass fibers, at least in that dimension, at that end point, behave like asbestos fibers, because

THE WITNESS: (cont'd.) we know that glass fibers can...and again, Dr. Morgan in his report used glass as well as asbestos fibers, and was able to show translocation patterns quantitatively different, but qualitatively similar for vitreous fibers.

So that the question of durability and the production of stigmata of exposure for manmade vitreous fibers stand in marked contrast, because as was pointed out here earlier, the inhalation of asbestos fibers, to a remarkable degree, those that are retained are going to be there for a long time - some are going to be there.

So that the issue of substitutes using other fibers has to take into account dimension, dose and durability, with durability perhaps being the critical discriminant.

DR. UFFEN: Could you pursue the point that you made about the rate at which the fibers can be dissolved by the tissue juices is different? Is it really significantly different, or moderately different?

THE WITNESS: It is significantly different but only in test tube conditions, in in vitro systems. We have no data, we are getting this data now in studies that are currently going on in three national laboratories in the United States, studies supported by the vitreious fiber industry, studies that are going on at Brookhaven National Laboratory, studies that are going on at Los Alamos National Laboratory and the Sandia Laboratories in Albuquerque, New Mexico, where a series of inhalation studies of precisely defined fiber are in progress, where three modes of application are in progress - one is a cloud inhalation, the other is intratracheal installation, and so as to make sure that none of...that something out of phase with the earlier studies of Stanton, of that type, are done as well.

So it's really an alpha to omega approach to vitreous fibers.

THE WITNESS: (cont'd.) So it's in these animals that we are going to show dissolution as well in an intact system, in an in vivo system.

But on a test tube basis, we can say that manmade vitreous fibers...and it's compatible with the noncrystalline structure of the fiber...are more susceptible to dissolution.

DR. UFFEN: One little final followup to it. Would that have, theoretically, there is no data available, an effect on a potential latency period for manmade fiber? Could there be a latency period?

THE WITNESS: It would be a miracle if there weren't. Yes, sir, there would be a latency period.

DR. UFFEN: Have you got any idea what it might be?

THE WITNESS: Well, let's just arbitrarily use the asbestos as the...let's use that as the norm, and we know that the latency period for...then you get into the long end of the spectrum for mesothelioma, and it can be a third and fourth decade subsequent to the onset of exposure. Asbestos is more nearly a decade and a half to two and a half decades, and asbestosis, fibrosis would be a significant part of the single decade segment...all of them with the caveat of biological variation.

So this is where we stand on manmade vitreous fibers, which clearly are one of the things we have thought of as a fiber for commerce and industry.

DR. DUPRE: Dr. Kotin, do the studies of the dissolubility of vitreous fibers that are no ongoing include the opportunity of once again trying to verify or otherwise the relative degrees of dissolubility of different kinds of asbestos fibers?

THE WITNESS: Absolutely. They are all part of the same protocol.

DR. DUPRE: So these studies, among other things,

DR. DUPRE: (cont'd.) would shed somewhat more light on the hypotheses that deal with relatively greater or lesser dissolubility, say of chrysotile in relation to amphibole?

THE WITNESS: Clearly, and if Dr. Wagner were to come, he...I'm unaware of any real studies on either mechanism or assay for manmade vitreous fibers that do not have, within the limits of the capability of the institution or the experimentalist, an asbestos control. Because basically the infinite knowledge we have about asbestos compared to the exceedingly limited knowledge we have about vitreous fibers, as you suggest, sir, would almost be derelict if they didn't have that kind of control.

DR. DUPRE: Dr. Mustard?

DR. MUSTARD: I would like to combine epidemiology and biology for a moment, and remind us all that Dr. Sackett, when he spoke to us about the principles of epidemiology design and measurement said that associations demonstrated in epidemiology were weak unless they had biological credibility. Obviously that's the linkage we are trying to make here.

If I may, I'm going to refer to the Lyon Conference...and I'll give the page number and volume...and also to the Brody article which you distributed yesterday, which is tab something-or-other.

DR. DUPRE: Exhibit thirty-two.

MR. WARREN: Exhibit thirty-two.

DR. MUSTARD: If I turn first to the Brody article on...the page number I can't find, but I'm sure it's 674...on the righthand side, he has a description about fibers and where they go, and one of the nice things in his presentation, which I see is in other papers, is that the fibers, of course, are not only taken up by the macrophages, they are also taken up by the cell's lining, which has some significance.

But one of the points he makes is that the longer fibers tend to be sort of distributed down the airway, and that

DR. MUSTARD: (cont'd.) taking thinness into account, the shorter fibers tend to be coming down into the alveoli, which raises a question for me and that is that it's the longer fibers, I would presume, that the macrophage is going to have trouble getting completely around.

THE WITNESS: Yes, sir.

DR. MUSTARD: Which raises the question in my mind about if we are assuming that if the fiber...macrophage battling with a fiber, or maybe an epithelial cell battling with a fiber that it can't get around, that may be part of the biological effect that produces the neoplastic change, has anybody done a careful study both in human post mortem material and in the animal experiments about the sites where the cancers originate in relation to the distribution of the fibers?

THE WITNESS: Yes, they have, but...well, let me put it this way: About the sites in relation to inhalants, it hasn't been done for asbestos. It has been done for the inhalation of particles carrying radon and its daughters. It has been done in the uranium miner population. It has been done in the populations that date back to the earlier studies of Doll and Hill on gas retort workers and gas workers in London, and then... where an increased risk to lung cancer was observed.

Then it's been done with cigarette smokers as well, and there Dr. Oscar Auerbach did the monumental study.

DR. MUSTARD: The one thing is, I have the impression that the fibrosis tends to occur down around the smaller parts of the airways, the alveoli and whatnot, and what I was just wondering is if there might be some disassociation between the sites of maximum fibrosis and the sites where tumors develop in the pulmonary tree?

THE WITNESS: Not really. I think there is rather a universal agreement among pathologists that the initial site of fibrosis is peribronchiolar, and it's the bronchiolar epithelium

THE WITNESS: (cont'd.) that gives rise, as I have said, I believe, to the neoplasm. So there is this apposition, as it were, because the interstitial fibrosis is really a radiation of fibrous tissue along the scaffolding of the alveolar septa are destroyed.

But it is interesting, the only hooker in all those studies is, when you get to the cancer. One of the interesting phenomena in lung cancer has been that from the year 1940, let's say, to the year 1970, the site of origin of cancers has been moving more and more peripheral. Not because there has been any delay, any change in the biology of carcinogenisis, but we are getting at these cancers so much earlier that we are beginning to see them at a time when they are much closer to their site of origin.

Initially, people...I mean the treatment of cancer was at a time when it had invaded both peripherally and centrally and your central tumor mass...if there is such a thing, it's a term that Professor LeBeau coined...if there is such a thing, has been moving more and more distally because of the fact that we are getting to see the tumors much more early in their natural history, as a reflection not only of cytology, but occupational screening with x-ray and the like.

But there have been these studies and there is this correlation between deposition and site of the sequence of hyperplasia and metaplasia, atypism, in situ and invasive cancer.

DR. MUSTARD: So the Brody article, in your answer, would all be compatible with the hazard site is the site where you have fibers that localize, that the macrophage or epithelial cells cannot surround, and it's at that site that you will tend to get both the tumor and the fibrosis?

THE WITNESS: I believe so, yes. In the data, it was an interesting paper, and...

DR. MUSTARD: Now, if I can turn to the Lyon book, volume one, and the series of articles in there on animal experimentation - Davis, Wagner and others.

There is an interesting reference to the effect that smoking...which is in Jones' summary, which I think is page 377, in which he comments on the fact that, "The animal experimental

> work has been unable to satisfactorily demonstrate a synergism between smoking and asbestos fibers".

You are aware of that one?

THE WITNESS: Yes.

DR. MUSTARD: That's a fascinating sort of problem because I wondered in terms of my Sackett Hypothesis about biological credibility if there couldn't be some interesting questions that one could pose out of this.

One of the questions that occurred to me is that it's very difficult to get animals to actually put cigarettes between their lips and inhale them and get the full impact of all the things that come from combusion of paper and tobacco. The sort of thing I was wondering about, is that the explanation for why the animal experiments have not succeeded? It's my understanding the experiments have required the animals to smoke by something else, that it's a secondary inhalation that they are getting.

Is that the difference, do you think, between the reason why the animals have not shown a susceptibility to synergism, or is it something else?

THE WITNESS: I really don't know. I think that in the one experiment where animals did smoke...in contrast to the virtually universal way that you describe...was the study of Oscar Auerbach and Robie, where they performed tracheostomies, put holes in the windpipe of the animals, and actually then in a positive way blew smoke down the tracheobronchial tree. They were unable to produce malginant neoplasms. They produced the whole sequence of changes, but up to malignant neoplasms.

THE WITNESS: (cont'd.) I think the lack of synergism is a reflection of the constancy of smoking, it's a dose response. There is no way you can get an animal...first of all, there is a difference that has been observed in the susceptibility of animals and man to the effect of the alkyloids, the three major ones, in terms of toxicity, and with the advent of low-tar and low-nicotine cigarettes, there is a whole new series of experiments being begun...I think in Hanford, Washington, where they may have an answer to this question because this will circumvent...it will still have carcinogenic materials in it, but it will circumvent the toxicity of the alkyloids that have been a limiting factor in experiments in the past.

DR. MUSTARD: Can I ask a question about the distribution of tars when people smoke? Do they tend to localize in the lower parts of the lung, or not? Do you know the evidence on that?

THE WITNESS: Well, you find it throughout the respiratory tract. If you scrape with a tongue blade the oral mucosa of a smoker and put it under fluorescent light, you will see the fluoresence of the polycyclic hydrocarbons.

But clearly, as I'm sure you have seen many times, the engorged macrophages with tobacco pigment are found at the level of the bronchioles, the alveolar ducts and the alveoli.

DR. MUSTARD: Do these tars tend to associate with fibers? Has anybody done any studies to look at the association between ...?

THE WITNESS: Yes. There have been several studies to see, because of the fact that you have a highly absorptive surface inthe asbestos fiber, there have been efforts to study how the tobacco will..both the pure carcinogenic hydrocarbons as well as tobacco, and clearly an asbestos fiber coated with benzpyrene, let's say, will have a synergistic effect.

THE WITNESS: (cont'd.) It will be more than just one plus one equal two.

So that one can demonstrate microscopically the adherence of cigarette smoke aerosol materials to an asbestos fiber.

DR. MUSTARD: So there could be some kind of mutual localization phenomona that occurs?

THE WITNESS: Yes, sir.

DR. MUSTARD: Which leads me of course to another very wild speculation in terms of the Sackett Hypothesis, of course, it might be that there isn't actual synergism in the lungs between the product of cigarette smoke and asbestos, but if you smoke your respirations may be changed and you might in effect inhale more fibers. Has anybody looked at the pulmonary dynamics of asbestos workers in terms of this particular problem?

THE WITNESS: Not that I'm aware of, no, sir.

DR. MUSTARD: I know that's far out, but you have to think of all the possibilities. I'm sure that if you worked in an asbestos plant and you had to run up and down stairs, that you would inhale more fibers than a person who doesn't have to do that.

THE WITNESS: Absolutely.

DR. MUSTARD: One final question, the question of lymphosarcoma has come up occasionally in these hearings, and you described very nicely how the lymphatics drain the lymph nodes. Do you have any views about the induction of cancer in the lymph nodes by asbestos fibers?

THE WITNESS: Yes, sir. There have been three specific studies in animals, and the epidemiologic studies would have perforce looked for lymphosarcoma. It's peculiar in the sense that if one were to expose animals to vitreous fibers, and an equal amount of nonvitreous fibers or crystalline fibers, you would find that vitreous fibers are...will engorge

THE WITNESS: (cont'd.) the regional lymph nodes and you can see them for long periods afterwards.

It is relatively uncommon to find, no matter how heavily the exposure has been to asbestos in the past, occupationally, it's relatively uncommon to find a really heavy concentration. You will notice in the picture there, lymph nodes with asbestos fibers in them are the exception rather than the rule.

This is, I think, not nearly as enigmatic as it might sound. First of all, the long, thin fibers would have a little trouble getting through and they are not as maleable, and above all, they are not fractured the way glass fibers are, and I think the work of both Davies in Edinburgh, and Kueschner and Wright, have clearly shown that there is this horizontal fracturing of the fibers.

Now as to why you don't get lymphosarcoma, I have no knowledge other than the fact that you don't, and it's one of the remarkable things about asbestos in the sense that here you have a tissue that is rapidly dividing, highly susceptible to other carcinogens. Ionizing radiation, for instance, preferentially will produce neoplasms of the lymphatic system.

So I don't know, but it just isn't there. Selikoff has looked for it, the people in South Africa have looked for it, the people in the U.K. have looked for it, and I think it's fair to say that in the most recent New York Academy of Sciences and a new book by Rosenoff, Dr. Selikoff in addition to listing positive associations has taken the trouble to identify a list of negative associations, and lymphosarcoma is included in the negative associations.

DR. DUPRE: Dr. Kotin, I just have, I think, a very brief line of questioning which is simply intended to provide me with my own personal review of the biology 101 presentation that you gave us yesterday, with respect to lung cancer and

DR. DUPRE: (cont'd.) asbestos.

Yesterday afternoon as I listened to the testimony that you were developing for Mr. Warren, I sensed as I listened that what you were saying might enable you to almost come to the conclusion that asbestos has very little to do with lung cancer.

Then, of course, especially as I listened to your testimony and your dialogue with Mr. Laskin this morning, I realized that no, this was not where some of yesterday afternoon's presentation was taking us at all, at least in the sense that I understood you quite clearly to say that asbestos, of course always given some appropriate dose, will indeed induce cancer... for example, induce cancer in a nonsmoker.

Now, to try once again to square that one with what I was...or what I thought I was learning yesterday afternoon, let me ask you this: Can I just try to use the verbs of inducing and of promoting. Now, looking at lung cancer in the smoker, would it be legitimate for me to take away the following from yesterday afternoon's presentation, which would be: That in a smoker there is perhaps a fairly high likelihood that asbestos will promote the development of cancer, which however has been induced by the smoking?

THE WITNESS: If I make one comment: Because of the fact that induction and promotion have such precise terms in carcinogenisis, would you let me substitute the words the determinant and the modifier, and indeed cigarette smoking would be the determinant and asbestos the modifier. Because as I say, the other terms are very precise terms.

Now that really was essentially a theoretical and a highly-creditable theoretical position until some recent data, data that are now some two or three years old, from Mount Sinai, in which Dr. Hammond and Dr. Selikoff reported that the initial observation made many, many years ago on smokers alone that cessation of smoking, after the passage of time, measureable in

THE WITNESS: (cont'd.) quinquennia, was associated with the reduction in risk. So that I think Dr. Hammond's position was that if you were fortunate enough to have stopped smoking for fifteen years, let's say, and had not developed a bronchogenic cancer, you essentially were at a risk level equal to that of a person who never smoked. You had essentially repaired, and the reversibility that I just described...

Now, nobody could have believed that, because first of all there weren't all that many exsmokers, until an analogous study of the Royal College of Surgeons, the Doll and Hill study, essentially found the same...that cessation of smoking was associated with the reduction of risk.

Well, again, the medical role that the Mount Sinai group had for the insulation workers, even though it was only a population of seventeen thousand, but really represented close to a third to a half a million manyears of exposure, they were able to prevail upon many, many of the workers to stop smoking, and again they found peculiarly enough, though the amplitude of the curve was less, the shape of the curve was exactly the same for asbestos cigarette smokers as it was for cigarette smokers alone.

Cessation of smoking, while indeed...well, let me begin again...cessation of smoking was associated with a reduction in risk to lung cancer that, measured by five year periods, showed a reduction to where, at the end of a nine year or a ten year...I think it was a ten year period Dr. Selikoff has published... that those workers had half the risk of that which they had at the time they stopped smoking.

The second thing that was of interest in the observations of the Mount Sinai group was that cessation of smoking in workers who had had fibrotic changes really didn't alter that, didn't significantly change that group from the other group. The course of asbestos-related asbestosis varied in that population that stopped smoking from some group where the

THE WITNESS: (cont'd.) progress was inexorable...it just went on...and others where it really made no difference, they continued to work and whatever change they had was static.

But the important thing was, in the workers who had stopped asbestos exposure no analogous reduction in lung cancer risk could be found.

Again, the numbers...I wish we were dealing with a hundred and seventy thousand people rather than seventeen thousand people, but nevertheless, that's the case.

But in asbestos workers, as I say, this was not.

All right. What we know about carcinogenisis is that removing the modifier will not have the amplitude of effect that removing the determinant will, and clearly the conclusion from the data...and similar studies are now going on on other very large populations...the removal of the determinant would only mirror the determinant role in cigarette smokers who have never been exposed to asbestos occupationally, if in fact it were the determinant rather than the modifier...because a modifier has a modulating effect, but it really doesn't have, as in the case of cigarette smoking where the role of the promoter is really not all that important in the sense that cigarettes... the complex of cigarette smoke has the inducer and the promoter. But one of the early experiments and one of the early enigmas in cigarette smoke and carcinogenisis was that if you were to add the carcinogenic potency of the known carcinogens, the polycyclics, the heterocyclics, and take all these materials and then use a painting or an injection experiment, you couldn't get as many...you would not get with the chemical carcinogens as many neoplasms as you got with just cigarette smoke condensate.

All you have to do is look at the makeup of cigarette smoke condensate, which has phenols, polyphenols, acroleins, organic acids, all of which qualify as promoters, and

THE WITNESS: (cont'd.) in the case of phenols and polyphenols, we use them experimentally in the laboratories as promoters.

So that really the totality of evidence would, I believe, support the position...the epidemiologic evidence, the experimental evidence, the bioassay evidence and the mechanism evidence...that cigarette smoking is a determinant and asbestos is a modifier. There is no questioning the enhancement and modifying role of asbestos on the cigarette smoke.

DR. DUPRE: Well, Dr. Kotin, you are by now, with your second appearance, a veteran of this Commission. You have, of course, and we are very grateful for this, an opportunity to acquire further hash marks in our purpose, and I thank you for the last day and a half, very, very much indeed.

THE WITNESS: I thank you for inviting me. Thank you very much.

DR. DUPRE: Counsel, I assume that we now rise until ten o'clock tomorrow morning, is that correct?

MR. LASKIN: Yes.

DR. DUPRE: Thank you.

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THE INQUIRY ADJOURNED

THE FOREGOING WAS PREPARED
FROM THE TAPED RECORDINGS
OF THE INQUIRY PROCEEDINGS

Edwina Macht

EDWINA MACHT